A. L. Loomis

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Vivesection

THE

Influence of Animal Experimentation on Medical Science.

By A. L. LOOMIS, M. D., LL.D.

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THE INFLUENCE OF ANIMAL EXPERIMENTATION ON MEDICAL SCIENCE.

GENTLEMEN:—This third meeting of the Congress of American Physicians and Surgeons is a most memorable occasion, since it has established the success of an undertaking, which aimed to unite in one representative body groups of acknowledged experts in all departments of Medicine and Surgery. It is, however, no longer an experiment, for the record of work done places it high in the list of scientific associations. Its broadening influences upon American Medicine and Surgery have already been felt and acknowledged. The vast extent of modern medical research, the various objects of separate interest which it includes, and the limitations of human intellect, have made it necessary that there should be groups of workers in many different departments.

It is clear that one mind cannot advance medical knowledge except by an infinitesimal degree. In ages when strong minds were few and intercourse limited, men must needs have been more than human to have accomplished much more than their masters did. For nearly a thousand years the history of medicine may be traced by a few names. Schools were founded on men, not on principles, until loyalty to one's master, the founder of a school, became stronger than truth. Even as late as the sixteenth century, Galen, Hippocrates and the Arabic authorities were the teachers of medicine throughout the civilized world. From the crumbling ruins of abstruse theories and the wrecks of individual systems has come a scientific scepticism, which is to-day the most striking characteristic of medical thought,—a scepticism which doubts not for the sake of doubting, but which demands proofs and counter-proofs, which scans facts, not men, and which learns to recognize truth from whatever source it comes. It is this, which is making modern medicine truly scientific and giving to modern investigation an individuality which thinks and decides for itself. It is this spirit, this love of truth, dominating such gatherings as this, which, during the past two decades, has been shaping medical

thought and investigation. It is this keeping in close touch with one another's work that is giving to modern medicine its freshness, special activity in investigation and rapid growth, which is inspiring medical workers with a community of thought and action, and which is bearing fruit of the greatest promise. On such an occasion as this, in the presence of so many trained and skilled workers, it seems fitting that I should direct the current of thought to the lines of investigation which have made the discoveries of the last quarter of the nineteenth century possible.

From the beginning of history until the present century, medicine has been either absolutely denied a place among the Sciences or else branded as inexact, empyrical and laggard in its development and progress. Although dealing, as it does, with the most complex problems of human existence, where, as in no other science, every law of nature is controlled and modified by that unknown force we call *vitality*, Medicine has nevertheless, from the very first, been forced to meet the demand for complete knowledge. To it alone, the answer "we do not yet know all" has been denied.

No greater misconception has ever gained footing in the public mind than the belief in disease as an entity,—an evil spirit to be exorcised or driven out by drugs. The superficial observer recognizes only results and gross phenomena; he is content with knowing the end, never asking for causes. For him motion and quiescence as shown by his senses are the ultimatum; factors and forces have no place in his mental processes. Yet these are precisely what science seeks to define, and until he has made the first analysis of terms, established absolute variations of quantity and quality, and determined the fixed ratio of forces, the scientific worker is not content.

In determining then the influence of any one factor in the development of medical science, results cannot be measured by the perfection of the whole, but must be estimated solely by the degree of advance toward the completed investigations.

The specific problems with which medical science deals are thus seen to be questions of the relative influence of multiple forces on the production of given results. When Galvani recognized electric force in the twitching muscles of his dismembered frogs and Volta was led thereby to the development of apparatus for the continuous production of this mysterious agency, there was no hint whatever of the far-reaching influence of electricity in modern medicine. Yet history shows that one discovery was the direct result of the other and that every electrical device for the relief of disease has its origin in those quivering batrachian limbs.

Only the deepest ignorance can fail to recognize that the forces concerned in the simplest changes of inorganic nature are so numerous, and their relations so complex, that they defy recognition under uncontrolled conditions, while in the organic world the task is even more hopeless. Experimentation, therefore, in which one or more of the involved forces can be controlled or predetermined and eliminated, becomes an absolute necessity in all scientific investigation. However clear the mental analysis, however accurate the logical demonstration from cause to effect, it is possible by experiment alone, under controlled conditions, to prove that no involved force has been overlooked; that the premises were true and the conclusions therefore ultimate. The truly scientific investigator is an analyist and purist, who seeks to establish the values of single, in place of combined, forces. His results are therefore primarily isolated facts, and their value not immediately evident, often indeed their relations are so remote, and their values so contingent upon yet other undetermined truths that they gain but scanty recognition; if perchance they are not totally ignored, and finally forgotten. Meanwhile the brazen dicta of some mere observer, who only sees most superficial relations and blindly accepts an assumed possibility as demonstrated fact, gain unhesitating credence. Yet the scientific experimentator alone, adds to our store of knowledge and power for good. He seeks for truth and truth alone. However isolated or unrelated his results may seem, he sees in each a potential value. The smallest discovery thus not only has its own pecular merit, but points the way to other hidden truths, although it may often be difficult to connect the several links in the long chain of progressive knowledge.

The world might still be standing in dumb awe and barbaric fear of Jove's thunder-bolts, had not Franklin's kite decoyed the blinding force and locked it in his Leyden jar. Thus bound and under predetermined conditions of action, it was brought within the power of scientific investigation.

Is it not strange that Medicine should be denied the right to follow those imperative methods of scientific research which are so unquestioningly accorded to every other science?

It has been assumed that the medical investigator finds ample opportunity for experimentation in studying disease under the ordinary conditions of human life.

Recognition, however, of the fact that experiments are never isolated, but in continuous and consequent series; that unknown quantities are determined, as in solving algebraic equations, by successive eliminations, and that ultimate values are obtained only from experi-

ments involving but a single unknown term, at once indicates how uncertain, and hence valueless, conclusions drawn only from clinical experience must be. If further proof be desired it is found in the well-known uncertainty and variability of disease processes, and the associated systemic reaction. Scientific experimentation thus demands conditions under which the largest possible number of the involved factors can be controlled or known. For medical science these conditions can only be found in a healthy organism. This science must therefore either stand still, or investigate the mysteries of life, where life holds its myriad forces in perfect harmony. Thus, it seeks not primarly to discover cures for disease, but rather to separate the multiple factors of disease and to fix the relations of such factors to the forces under our control, by which they may be modified. It is not a little surprising that, with an appreciation of the necessity for experimentation, men should for so long have preferred to be its subjects, and that even to-day so many refuse to yield the place to animals. For example, in wide-spread epidemics we note the effects of an infection on perhaps half a million of human beings, with a great sacrifice of human life. On the other hand we study in laboratories the cause of the epidemics, with comparatively small sacrifice of animal life.

In entering upon the consideration of this subject I fearlessly lay down this proposition, confident that it states your unanimous verdict as representatives of medical science on this continent. That every distinct advance, every established principle, and every universally accepted law of medical science has been in the past and will be in the future the indirect, if not direct, result of animal experimentation. I ask you to review with me some of the more obvious and conclusive proofs of this proposition.

The imperative lines of our investigation may be broadly classed under four heads :

1. *Experiments to determine the functions and normal relations of the organs composing the physical economy.*

2. *The causes of those perversions of function present in the condition designated disease.*

3. *The nature of morbid processes and the relations of their causes to the consequent systemic reactions.*

4. *The protective and curative influence upon these processes of agencies under our control.*

In this review I shall follow an historical order, and present in an Appendix detailed accounts of all experiments to which reference is made.

It is not too much to claim that during the latter half of the present century the results obtained from experiments on animals have done more than all the observations of the preceding centuries to raise medicine from conditions of vagueness to conditions of exactness. From the time of Aristotle (1), who proved that the blood, brain and spinal marrow in animals have no sensation, down to the present day, animal experimentation has been practised by all investigators, who have gained any definite knowledge of the more important phenomena of animal life.

Galen (2), however, must always be regarded as the pioneer in this line of investigation. He may be said to have laid the foundation stone of medical science. By his experiments on living animals he showed that arteries contain blood, that the lungs passively follow the movements of the chest, and that the diaphragm, although the most important, is not the only muscle of respiration. Furthermore, by section of the spinal cord and the recurrent laryngeal nerve, he demonstrated the nervous control of the voice and explained the mechanics of respiration. By various methods he greatly advanced the knowledge of the structure and functions of the alimentary canal, demonstrated the movements of the stomach and the peristalsis of the intestines and laid the foundation of our present extensive knowledge of the functions of the brain and spinal cord. The results of his experimental work are "as conclusive now as when he first made them, and retain to-day their full value;" in fact they are the only part of his vast labor which has stood the test of modern investigation. The knowledge of the circulation and respiration which was gained by his experiments on animals in the second century was the foundation and a necessary preliminary to Harvey's complete discovery of the circulation in the seventeenth century. His experimental labor was the only work that has survived the fluctuating medical systems of the Dark Ages, with perhaps two exceptions, viz.: First, Vesalius (3), who in the sixteenth century created for medicine a solid foundation by transforming anatomy into an exact science, found that the action of the heart might be continued for some time by inflating the lungs of animals with air after the chest cavity was opened, and published, in 1543, his discovery of artificial respiration. Secondly, R. Columbus (4), in 1559, by direct experimentation on living animals discovered the pulmonary circulation. In fact, from Galen's time till Harvey's great discovery, with these exceptions little experimental work was done and during most of this period medicine instead of advancing towards a science became more and more the plaything of theorists and impostors.

Harvey (5) following the practice of Vesalius and Columbus, of making anatomical examinations of the living parts according to experimental methods, established, in 1620, his great doctrine of the circulation of the blood. As it has been frequently denied that his discovery rested entirely on animal experimentation, I have given in the Appendix his own quaint and detailed account of it, which I am sure is quite enough to silence all question on this point. By a long series of carefully conducted experiments on animals and by that alone, he unravelled the system of the circulation and established a discovery which, more than any other, influenced the future of medicine and surgery. It needed only the microscopic demonstration of the capillary circulation by Malpighi, (6) and his demonstration of the circulation in the lung of a living frog, to make the solution of the great vital problem complete.

The next series of important and epoch-making experiments on animals were applied by Galvani (7) and Volta (8) to the nervous system. Each investigator was in error in his explanation of the results obtained by his researches, but their great discovery was not lost on account of the wrong interpretation which they gave to it, for their experiments on the electric condition of the nerves and muscles of animals established an epoch in the history of the physiology and pathology of the nervous system, which led to brilliant results a century afterwards.

The first attempt to continue life for an indefinite period by artificial respiration was made by Robert Hook (9), in 1664. He showed that "by inflating the lungs of animals with a bellows and then allowing them to collapse, an artificial respiration might be established which could be kept up for a long period." Artificial respiration according to Hook's method was afterwards practised by Brodie (10) and others for the purpose of studying the action of the heart and blood vessels and for resuscitating asphyxiated animals. The principle established by these experiments on animals was later applied to the human subject and is now a recognized means of preserving life in cases of asphyxia and of resuscitating the newly born.

The countless experiments on living animals, carried on during the seventeenth century in all the medical centres of Europe, on the action of the heart, the circulation, absorption, secretion and respiration produced a fund of knowledge without which the brilliant advances of the eighteenth century would have been impossible.

By experiments on birds, frogs and insects, Boyle (11) near the close of the seventeenth century (1670) showed that atmospheric air is necessary to the maintenance of life, as he found that air which had

been breathed by animals for some time, became finally unfit for respiration so that the animals died.

Priestley (12) continued Boyle's experiments on air vitiated by respiration, establishing the fact that by growing plants in the vitiated air, it becomes regenerated and is again fit to breathe. It remained, however, for Lavoisier (13), following Hook's and Priestley's experimental methods, to establish at that time the true composition of atmospheric air and to develop the real basis of respiration; viz.: the absorption of oxygen and the exhalation of carbon dioxide. This discovery opened an entirely new field in the study of respiration and laid the foundation of our present knowledge of the respiratory processes.

The injection of fluids into the blood vessels of animals was first performed by Dr. Christopher Wren (14) of Oxford. He employed an infusion of opium and produced narcotism in the injected animals. His experiments in this line were soon followed by those of Richard Lower (15), who, in 1666, performed the first transfusion of blood in animals and the following year Dr. Denis (16) performed the same experiment on man. Mr. Boyle (17) afterwards elaborated the method of transfusing blood from one animal to another, and showed that death from hemorrhage might be prevented by such transfusion. These experiments led later to the establishment of the practice of transfusion for certain conditions of bloodlessness, a principle which to-day occupies a prominent place in life-saving methods.

After Galen's experiments on the nervous system of animals, the labors of investigators were chiefly confined to anatomical studies of the nervous system and little or no advance was made in the knowledge of its function until the middle of the eighteenth century, when Haller proved by numerous experiments in cutting and irritating nerves, "that all motion in the human body proceeds in a great measure from the brain and its annexed cerebellum and spinal marrow." He also demonstrated that when the peripheral end of a severed nerve is irritated the muscle to which it is distributed contracts. Soon after, Sir Charles Bell (18) commenced his experiments on the spinal cord and nerves of animals in order to determine the functions of the cerebrum and cerebellum, but after long labor reached no satisfactory result. Ten years later, however, while experimenting on facial nerves, in his attempts to demonstrate the existence of a great system of respiratory nerves separate from those of sensibility and voluntary motion, he established the important fact that the seventh cranial nerve is a nerve of motion and the fifth a nerve of sensation. This discovery has been fruitful of practical results both in medicine and surgery.

Although Bell did not believe in animal experimentation as a source of knowledge, and employed it only to prove or confirm his anatomical studies, nevertheless his experimental work is the only part of his labor which has remained. The classifications and fascinating theories which he so ingeniously constructed on the basis of his anatomical studies are hardly known to neurologists of the nineteenth century.

Magendie (19) inaugurated the present century by a series of most brilliant experiments. He recognized the dangers of adopting theories based on imperfect knowledge and devoted himself accordingly to eliminating these imperfections by experiments on living animals. "The love of knowledge for its own sake was the impulse which dominated all his work. He claimed that all science was inductive and consequently founded on experiment and maintained that the science of life necessitated animal experimentation."

By a series of carefully conducted experiments on the spinal cord, in which he divided successively the anterior and posterior roots of the spinal nerve, he demonstrated the difference between the motor and sensitive nerve roots. In this way the distinct endowment of the two kinds of nerve fibres was established. Once placed on this footing the study of nerve physiology was greatly increased in efficiency and extent. Thus, by applying the Galvanic stimulus to a spinal nerve above and below the point of section, its mode of action was determined by the excitability of its motor and sensitive fibres. He employed the same methods in the study of the cranial nerves, both externally and at their roots. In fact every branch of inosculation was scrutinized by the same means.

It is hardly possible to estimate the importance of the change thus introduced into the study of the functions of the nervous system and the facilities which were thus supplied for further investigation. "This distinction between the spinal nerve roots was of the utmost importance, for it indicated a general plan of arrangement for the nervous system throughout the body. It became immediately a subject of criticism and verification for all the leading investigators of Europe and the result was a complete acceptance of Magendie's discovery." Magendie not only cleared up much that was vague and uncertain in the physiology of the nervous system, but he established methods of experimenting on the action of medicinal agents and was the first to demonstrate conclusively that "poisons act on the spinal cord through the circulation and not by means of the lymphatics and nerves." His results, obtained by experiments on animals with strychnine, quinine, iodine and a long list of medicinal substances, enabled him to lay the foundation of the doctrine that remedies exert their special action

upon special structures and organs, a doctrine which was afterwards further developed by Claude Bernard and is now the accepted view regarding the action of all medicinal agents. He further demonstrated so thoroughly and clearly the action of strychnine on the spinal cord, that subsequent investigations have added but little to his results.

Magendie entered upon the investigation of all subjects with a sort of skepticism that demanded proof and counter-proof. In his studies of the functions of organs he was forced to experiment on animals and we may rightly regard him as the originator of the modern system of animal experimentation. Following the path which his great teacher had made so brilliant, Claude Bernard (20), by dividing the sympathetic nerve in the neck of the rabbit, observed that the bloodvessels in the ear of the corresponding side became enlarged and demonstrated by a series of similar experiments that the size of the bloodvessels is under the control of particular nerves which cause them to contract and dilate.

I demand from all opponents of animal experimentation recognition of the following fact. In all this long list of investigations not a single experiment was directed immediately to the discovery of a cure for a disease, but solely to the determination of physiological functions and the normal action of the vital processes, as indicated under the first head of our classification, and to defining the specific influence of given substances upon healthy living organisms, as indicated under the fourth head of our classification. It would have been impossible at that time even to guess just what valuable results were to come from these discoveries. Yet these experimentators fully understood, what every one must understand who expects to comprehend the purpose of medical science, that the practise of medicine is by principle and not by precept. Each worker recognized that the truth he sought was only a part of medical science and each by his discoveries marked an epoch in that science.

It were a task for days even to tell the things we are now able to do upon the basis of Bernard's discovery of the Vaso-motor nerves, and the story of the specific action of drugs is no shorter. It is probably a conservative statement to say that, excluding the medicinal foods, ninety per cent. of all our medication is made definite and valuable by this principle alone, which occupies the same position toward medicine as does Newton's Law of Universal Attraction toward Physics.

Although Brodie (21) had done much experimental work on the action of medicines without reaching any satisfactory results, it was not until Claude Bernard applied *his* experimental methods that the true action of drugs was fully understood. His work on

Digitalis offers a most excellent illustration of the relative values of the experimental and clinical methods of study. Numerous observers had previously recognized that digitalis made the heart's action slower and therefore regarded it as a cardiac sedative. This conclusion Bernard proved to be the direct opposite of the truth, showing, by experiments on animals in which the drug was the only disturbing force, that its effect is not sedative, but on the contrary, stimulating and tonic, rendering the action of the heart more powerful and increasing the tension of the bloodvessels. The rules for its use in disease were thereby revolutionized and the results obtained by the use of this drug in so many diseased conditions were for the first time made certain. The necessity of investigating the action of drugs upon animals, in which the experiments could be controlled and varied, was thus conclusively proven by Bernard's work; and his methods were soon adopted by other investigators, by whom our knowledge of the action of remedies has been made definite to a degree that could never have been attained by mere observations of their effects upon man.

Thus, modern Therapeutics, emancipated from the bondage of empyricism, stripped of its chains, in which every link of personal interpretation differed from its fellows, no longer wounding friend as well as foe by aimless blows in the dark, stands forth a young but growing Hercules, bearing in place of the old barbaric club a magazine rifle with telescopic and microscopic sights, the ammunition box of which holds not drugs alone but a manual of directions wherein are written the truths which our modern priests, offering sacrifices on the altars of science, have given to mankind to save them from their infirmities.

Still the tale goes on ; Magendie, Bernard and Longet established by their experiments the doctrine of recurrent sensibility, which was followed by the great discovery of Marshall Hall (22) of the reflex action of the spinal cord. He observed that after the removal of the brain in animals the limbs were still capable of motion and he showed by further experiment that the spinal cord acts independently of the brain as a medium of communication between the integument and the muscles. The same form activity was afterwards found to be very widely extended in the nervous system. Legallois (23) and Flourens (24) showed that the medulla has its own centres of reflex action and is either directly or indirectly an essential to to the continuance of life.

There is to-day no more important department of nerve physiology than that in connection with the vaso-motor nervous system. It has been studied and developed by many observers but, as just mentioned, was practically established by Bernard's experiments. It solved not

only some of the most important and difficult problems of physiology, but made intelligible many unexplained pathological changes. The relation of disturbances of the surface circulation to diseases of the internal organs, the mechanism of local congestion. The recovery of nerves from the exhaustion of over stimulation, by rest. The varying effects produced by different kinds of electric stimuli and much similar knowledge mark the fruit of a long series of experiments made along the line so clearly marked out by Bernard. Each one of these series rested on the work of some preceding experimenter; together they form a continuous line of development which can be traced directly to the work done in Galvani's laboratory in 1789.

We turn now to experiments falling more directly under our third class. It is extremely suggestive as well as interesting to note that the order in which these discoveries came most clearly indicates that all investigators were working toward the relief of human suffering as their one great object. Anatomy and physiology could not be ignored, but pathology and etiology were forced to give place to therapeutics.

John Hunter (25) in 1785, by his experiments on the arteries of dogs, established the fact that injuries to healthy arteries were soon repaired and that ulceration of arteries after ligature only occurred in such as were primarily diseased at the point of ligation. These experiments led him to apply the ligature, for the cure of aneurism, to the healthy portion of the artery above the point of dilation. For more than a century his experiments on canine legs have borne fruit an hundred-fold in saving human lives and limbs.

Hunter first learned by experiments on pigeons and young pigs, "that the growth of bone takes place mainly from the exterior and is probably produced by the nutritive power of the periosteum." Subsequently, this question was further examined experimentally by Howship (26), Flourens (27), Heine (28), Murray and others. Mr. Syme (29) endeavoured to ascertain "whether the periosteum possesses the power of forming new osseous substance independently of any assistance from the bone itself. He extirpated the middle portion of the radius of a dog with its periosteum and found, as Sir Astley Cooper had previously done, that after the recovery of the animal there was no bony union, but a ligamental band running from one extremity to the other."

Leopold Ollier (30), by transplanting portions of the periosteum, demonstrated the power of the membrane to produce new bone and showed that in the resection of bone, if the periosteum is left, new bone will be developed in from one to three months. Following the

teachings of his animal experiments, he introduced the operation of resection for diseased bone, one of the most important discoveries in surgery which inaugurates a new era in surgical procedure. The practical results of his discovery are to-day fully approved by surgeons in the management of injuries or disease of the bones and joints.

As we witness some capital operation performed at the present day without pain, almost bloodless, followed neither by fever nor suppuration, we may ask how far these great results are due to experiments on animals. The anæsthesia of chloroform was discovered through experimentation on a low form of animal life, the ant. The illustrious Simpson practised and perfected his use of chloroform on animals before he anæsthetised his first patient. While its discovery as an anæsthetic cannot be claimed as altogether due to experiments on animals, its great uses in surgery would be incomplete but for such experiments. The same is true of that other great alleviator of pain, the hypodermic, which was first used by Mr. Rand (31) on his sporting dogs. He says " I feared that hypodermic injections might excite suppurative inflammation in the subcutaneous tissue, but when I found from experiments on dogs that this was not the case, I gained confidence that justified their use on man."

Whether Ambrose Paré made experiments on animals before using the ligature on man is not clear, but all the steps which were necessary to perfect this discovery and all the other means for arresting hemorrhage from bleeding vessels, have been the result of experiments on animals by Hunter (32), Jones (33), Benj. Travers (34), Bryant (35) and a long list of eminent surgeons during the past century.

Robert McDonnell states that great as are these triumphal epochs in surgery, which have rendered operations painless and bloodless, the practical surgeon of to-day values even more highly those antiseptics which render convalescence after operation free from fever and suppuration.

These three great epochs alone are sufficient to exalt animal experimentation to the first place as a means of scientific advancement, nor can they be obscured by the the multitude of brilliant discoveries that are showering upon us with a bewildering rapidity in these latter days.

I cannot help again calling your attention to the peculiar significance of the fact that etiology, which by right should have come first in the study of disease, has hitherto marched but haltingly in the rear, because it must depend upon animal experimentation alone for its development. It is unfortunate that a false sentiment has sought by every possible means to retard and check the progress of those, who essayed this path of investigation.

The first step in this important field of research was taken in 1850, when a commission of the medical association of the "Eure et Loir" proved that splenic fever could be communicated from one animal to another by innoculation; and the first hint of bacteriological study was given when Davaine (36) and Rayer found constantly in the blood of animals so innoculated little thread-like bodies.

At about the same time Prof. Virchow (37) furnished definite knowledge of the inception and prevention of parasitic diseases by a series of experiments on animals to determine the origin, nature, mode of development and communicability of trichinosis. Through these investigations the medical profession first became aware of the existence of a fatal and heretofore unknown disease, and were at the same time made acquainted with its source and manner of production.

M. Villemin (38) inaugurated a new and important era in medicine when he established the fact that tuberculosis is an infectious disease. By laboratory experiments he found that general and fatal tubercular infection is produced in animals when they are inoculated with crude tubercular matter from the human subject. His experiments in this line were soon confirmed by other investigators and led directly to all the far-reaching results, determining the modes by which tubercular infection can be propagated. Villemin's discovery revealed endless possibilities and was followed by similar investigations of many infectious diseases.

The invaluable studies of Pasteur (39) introduced us into "a new world of strange knowledge." His insight into the doctrine of fermentation carried him far beyond the agencies of microscopic organisms in fermentative processes. He not only isolated and obtained pure cultures of these organisms but also studied their life-history, and by methods which had served him in all his previous investigations, placed bacteriological science on a firm basis.

He demonstrated that, if the cause of an infectious disease be a self-multiplying germ from the outside world, the habits of the living enemy can be studied in its outside relations and that definite knowledge may thus be obtained as to its biological affinities. No work has ever promised greater things to the world than does that of Pasteur.

The knowledge obtained by observation, previous to the middle of the present century, concerning the changes effected by disease now began to be examined from a new point of view. Pasteur's methods of experimentation were adopted and practised by investigators all over the world and his doctrine, that the cause of infectious diseases was to be sought in self-multiplying germs, was everywhere accepted.

The crowning glory of Pasteur's work came with the discovery of attenuation of bacterial toxic products, the possible results of which defy the imagination. In the record of human industry there is no work of richer or grander promise. Yet it is a work which, from the very nature of the case, was possible only by experiments on living animals.

The endless possibilities of research which the new doctrine of infection suggests to the mind of the pathologist was the beginning of the most brilliant era in the science of medicine since it has existed. It would not be possible in the time allotted to me even to refer to all the investigations which have been made along the line so clearly defined by Pasteur.

I must pass by even the list of diseases over which victory has been made possible, in order that I may speak briefly of those in which practical results are already attained or in sight. The time is here when abstract scientific principles are bearing concrete fruit in the prevention and cure of disease.

The application of Pasteur's doctrine by Mr. Lister to the antiseptic treatment of wounds, an application which was enforced by Mr. Lister's eminent skill as an experimenter, has been a full confirmation of this principle. The germs which Pasteur imprisoned in his test-tubes were liberated by Lister's genius. Together they have put to flight the horrors of surgery and forever stand guard when the surgeon plunges his knife into the sleeping flesh or binds up the torn and mangled body.

The discovery of the bacillus tuberculosis by Koch (40) marks another brilliant epoch in medical science. The details of the work by which he reached this great discovery are too familiar to be repeated here, but it was only accomplished by Pasteur's method of continuous animal experimentation. It has not merely revolutionized our knowledge of tuberculosis, but has enabled us to understand and explain the morbid processes of tubercular disease. The stimulus which Koch's work gave to investigation in all countries is bearing fruit in the department of preventive medicine and therapeutics. The light which flashed from his laboratory was the dawn of hope that is already breaking into the day of certainty, when we shall hold a prevention and cure of tuberculosis in our grasp.

Following the line of Pasteur's work on the attenuation of bacterial toxic products, Kitasato (41) and Behring (42) in their experiments on the immunity and cure of tetanus have given definite knowledge of the prevention and cure of infectious diseases, which goes far towards the realization of the hope inspired by the work of Koch on the toxic products of the bacillus tuberculosis.

Within the past two decades animal experimentation has accomplished more in the field of cerebral localization than all the preceding centuries of carefully recorded cerebral symptoms studied in the light of post-mortem observations. It has opened to surgeons an entirely new field of operations. Until the middle of the present century the brain was described as a single organ and physiologists attributed to its functions no special localization. To-day the areas of motion and of special sense, and to a limited extent the mental areas also, have been definitely placed. Most, if not all, of this knowledge has been derived from experiments on the brains of living animals. From the time when Fritsch and Hitzig (43) reported their faithfully recorded and startling experiments in this new field of research, giving such complete details of their experimental procedure that other investigators could easily follow and test their accuracy, numerous workers have been adding to our knowledge, until we now have definite and safe rules by which we may localize many cerebral lesions. Any discrepancies which have been claimed as invalidating this line of work Dr. Ferrier (44) states will be found on careful examination to be more apparent than real and that experiments on animals under conditions selected and varied at the will of the experimenter are alone capable of furnishing precise data for sound inductions as to the functions of the brain in its various parts.

The surgeons have not been slow to make this knowledge practical in skillfully-devised operations. The region beyond the skull is no longer forbidden ground. The hopeless because powerless inactivity, that once watched in wondering silence the meaningless signs of conflict within the mind's temple, has now given place to a keen activity that boldly enters the inner court to seize the offender even at the base of the altar.

As we review the history of the experimental work which has placed medicine in the list of the sciences we are impressed with the fact that while each line of research was carried on for its own results, nevertheless most of the discoveries remained apparently barren until subsequent discoveries invested them with an unexpected importance.

The fatal error of the critics of experimental work is their demand that every experiment shall bear fruit immediately; few if any of them seem to be familiar with scientific methods. They constantly wander from the real issues to the moral or morbidly sentimental aspect of the question.

It seems evident from the history that I have spread before you in this brief and fragmentary manner, that most, if not all, of the real advances in medicine have been made possible through experimenta-

tion. The only point open to discussion then, from either moral or ethical point of view, is what price should be paid by the world for the benefit received. This review of what our profession has thus far done to serve mankind in this field is not a plea for mercy, not a bribe to tempt a captious public. My voice has proved a recreant servant if any tones of doubt or fear have marred this exposition. Its every part is cause for pride. In such a sketch, however cursory it may be, each point reflects the light of noble purpose and overflows with promise of better things to come. So long as the moral and spiritual development of mankind remains the supreme purpose of creation, medical science can claim equal honors with the science of God and in the conflict with physical evil must be the first to meet the foe. Until Infinity repeals the edict which gave man power over all created things, the right to claim the service of the brute creation, although it takes the life of the animal or tears it limb from limb, can never be denied to him who devotes his life to the service of mankind.

In this defence of animal experimentation results have not been made prominent with any purpose to conceal methods. We are fully prepared to count the cost and to meet the question "does the end justify the means?" As devotees to medical science, we yield precedence to none in honesty and lawfulness of purpose, or faithfulness of service in the bitter conflict humanity ever has waged and ever must wage against pain and disease. We too have hearts that love and pity, that ache and sometimes even break beneath the loads they bear. We glory in our experimental work because we know the tenderness of cruelty, the balm of pain; the life whose birth is only in the throes of death. Must then our conflict cease? our weapons be laid aside because selfish ambition has now and then made fiends of men? Since philosophers first learned to trace "with their golden pen on the deathless page" heroic deeds of men, humanity has never failed to offer its first homage to those who gave their lives for others. As the servants of such a science we can fearlessly appeal to all intelligent men for a just criticism. From the ignorant we expect to receive only censure, but from those who in "the valley of the shadow of death" have learned to know what manner of men we are, I have faith to believe the reply will come; *We have trusted you with the lives of our loved ones; we entrust to you God's dumb creation.*

APPENDIX.

(1)

Aristotle,* History of Animals. Aubert and Wimmer's Edition.

Book II, Chapter II, Section 44, vol. i, p. 272. (In the Chameleon) "when cut open, respiration continues active for a long time, and there occur very slight movements in the heart; and contractions take place not only, and especially, in the region of the ribs, but also in the other parts of the body."

Book III, Chapter XIX, Section 90. "In no animal has the blood any feeling when touched, any more than the excretions in the belly; nor has the brain or marrow,† when touched, any feeling."

(2)

On Practical Anatomy and Experimental Physiology. De Anatomicis Administrationibus. Galeni Opera Omnia, Kuhn's Edition, vol. ii, pp. 651–706.

An in Arteriis Natura Sanguis Contineatur. Galeni Opera Omnia, Kuhn's Edition, vol. iv, p. 703. Is blood naturally contained in the Arteries?

"For we have often exposed the large arteries convenient for this purpose, and asked the disciples of Erasistratus whether the artery thus exposed did not seem to contain blood. They were obliged to confess that it did, both because Erasistratus asserted that the blood passed into the arteries when they were uncovered, and because the fact was evident to the senses; for having placed ligatures on both ends of the inclosed portion of the artery, and made an incision into the vessel, between them, I showed that the artery itself was full of blood."

Book VIII, Chapter II. "There is a form of respiration which is considered to be a natural (i. e. involuntary) as opposed to a psychical (i. e. voluntary) function, and in which the lower parts of the chest and hypochondria are seen to be plainly in motion, but the upper parts sometimes not at all, and sometimes obscurely. This is accomplished by the diaphragm alone, which is a muscle not only in structure but in function also."

"But our teachers were wrong in believing the diaphragm to be the sole mover of the chest in respiration, expanding it when itself in contraction, and when itself in relaxation permitting the chest to collapse; for they did not explain how we are able to blow out vigorously or to vocalize. They thought that even the ample movements of the chest, which we see in running and in all such sharp gymnastics, are accomplished by the energy of the diaphragm." Galen goes on to say that no account was taken of the intercostals or muscles of forced breathing.

* The extracts from Aristotle, Galen, Vesalius, Columbus, and Malpighi were kindly furnished by Prof. J. G. Curtis from his library.

† The word marrow *μυελός* is used by Aristotle indifferently for the marrow of the bones and the spinal cord, the functions of which latter were unknown to him.

Book VIII, Chapter III. The technique of the dissection and experimental physiology of the muscles of respiration is here given, and the anatomy of the two sets of intercostals is described. The experiments are done on pigs because their voices are so strong that effects can be well observed.

If the external intercostal muscles are divided first and then the internal, the voice and forced breathing are abolished.

Galen uses large pigs, so that opening the pleura may be avoided, and advises one to practice well on the cadaver before experimenting. This demonstration of the use of the intercostal muscles Galen claims as new and original with him.

Book VIII, Chapter IV. Next he proves that the intercostal muscles owe their power to the intercostal nerves. For this purpose all these nerves are exposed near the spine and ligatured, but not so tightly as to bruise or sever the nerves. The ligatures on the nerves, if moderately tight, (1) paralyze the intercostal muscles, (2) prevent forced breathing, (3) abolish the voice. All these functions return when the ligatures are removed.

Book VIII, Chapter V. If the nerves now called the vagi are destroyed a hoarse sound like a snore may still be produced; but if the intercostal muscles are paralyzed, there is no hoarse sound at all.

Paralysis of the intercostal muscles may be effected not only by (1) section of their fibres, and (2) injury of their nerves, but by (3) excision of their ribs, and by (4) section of the spinal cord at the beginning of the back, between the seventh cervical and first dorsal vertebræ. This section of the spinal cord is found to paralyze every muscle below except the diaphragm, and also to render the animal voiceless. In an animal breathing only by the diaphragm, after section of the spinal cord at the beginning of the back, section of the phrenic nerves is seen to be followed by the contraction of certain accessory muscles at the upper part of the chest. In another animal Galen cut the phrenic nerves in the neck, and found that while the diaphragm was paralyzed, the intercostal muscles continued to act. In experiments where the spinal cord was cut at the beginning of the back, the upper and lower parts of the thorax might be seen to move, the lower by means of the diaphragm, the upper by means of accessory muscles.

In Book VIII, Chapter VI, the technique of cutting the spinal cord is given minutely. Galen sometimes used sucking pigs for this purpose. "When the spinal cord is divided longitudinally from above downward, directly in the middle line, not one of the intercostal nerves is paralyzed, either to the right or left, nor the lumbar nor crural nerves. But if the cord is divided transversely, only one-half way on either the right or left side, all the nerves of the injured side are immediately paralyzed." Hemisection of the cord reduces the volume of the voice one-half; complete section produces complete aphonia.

Book VIII, Chapter VII. Excision of the ribs destroys forced breathing and the voice as much as section of muscles or of nerves. Galen describes the technique of this excision. It must be subperiosteal and he cautions against piercing the pleura. The impression received is that *not all* of the ribs are to be removed.

Book VIII, Chapter IX. Section of the spinal cord at its commencement, or below the first, second or third cervical vertebræ totally paralyzes respira-

tion, and the whole of the body below. If below the sixth vertebræ the animal can still use the diaphragm, and if cut further down, other muscles of respiration remain intact: the lower the section, the greater the number.

(3)

Andreæ Vesalii, Bruxellensis, 1543. De Humani Corporis Fabrica. Lib. Septem, De Vivorum Sectione.

"In order that the life of an animal may be restored, an opening should be made in the trunk of the aspera arteria (trachea), into which a canula of reed is inserted and this blown through. For on slight inflation in the living animal the lung swells up to the size of the thoracic cavity, and the animal breathes after a fashion. The heart then resumes its force, and its motion varies with beautiful diversity. The lung being inflated from time to time, the motion of the heart can be well examined, both by sight and touch, and the trunk of the great artery [aorta] which extends along the back can be examined also in the thoracic cavity, or as far as the lumbar vertebræ.

"Nothing appears more manifest to you than the rhythmic beat of the heart and arteries, which being observed for a time, the lung should be inflated again. By this artifice, than which nothing I have discovered in experimental physiology [literally anatomy, but with more than its present meaning], pleases me more, much knowledge of the changes in the pulse may be obtained. For when the lung has remained flaccid for a time, the pulse or motion of the heart and arteries is seen to be undulating, creeping or vermicular, but the lung being inflated the pulse becomes large and rapid and shows remarkable inequality.

"I may say that this is the experiment by which I demonstrate to the best advantage to the candidates in medicine the nature of every kind of pulse."

(4)

Realdi Columbi, De Re Anatomica. Venetiis, MDLIX. p. 177, l.10–20.

"There are two cavities in the heart, that is two ventricles, not three as it seemed to Aristotle. One of these is to the right, the other to the left; the right is much larger than the left and contains natural blood, while the left contains the vital. Moreover, it is easy to satisfy one's self by observation that the substance of the heart which encloses the right ventricle is thin, and that the left is thick; this is partly for the sake of equilibrium, and partly in order that the vital blood which is very thin may not exude. For between these ventricles there is a septum through which almost all think that a passage is open for the blood from the right ventricle to the left, and that the easier, because on the way the blood is attenuated for the purpose of the generation of the vital spirits. But they are much out of the way; for the blood is carried through the pulmonary artery to the lung, and there undergoes its attenuation; thence along with air it is carried through the pulmonary vein to the left ventricle of the heart; which fact no one has hitherto noticed, or left recorded, although it is most worthy of the attention of all."

p. 178, l. 31-38. "Indeed I think just the opposite; namely, that the pulmonary vein is to carry blood mixed in the lungs with air to the left ventricle of the heart; which is as true as truth itself; for if you will examine not only in the cadaver, but likewise in the living animal, you will find always this [vein] filled with blood, which would by no means be the case if it were merely for air and vapors."

p. 224, l.16–21. "Verily I beseech you, oh candid reader, studious of the learned, but most studious of the truth, to experiment upon animals and to dissect them alive; try, I say, whether what I have said agrees with the facts; for in these animals you will find the pulmonary vein full of blood, not filled with air or smoky fumes, as they call them, please God! Only the pulse is lacking."

(5)

Harvey's works. Sydenham Edition, p. 19.

"When I first gave my mind to vivisections as a means of discovering the motions and uses of the heart, and sought to discover these from actual inspection and not from the writings of others, I found the task so truly arduous, so full of difficulties, that I was almost tempted to think, with Fracastorious, that the motion of the heart was only to be comprehended by God. For I could neither rightly perceive at first when the systole and when the diastole took place, nor when or where dilation and contraction occurred, by reason of the rapidity of the motion, which in many animals is accomplished in the twinkling of an eye, coming and going like a flash of lightning; so that the systole presented itself to me now from this point, now from that; the diastole the same; and then everything was reversed, the motions occurring, as it seemed variously and confusedly together. My mind was therefore greatly unsettled, nor did I know what I should myself conclude, nor what believe from others; and I was not surprised that Andreas Laurentius should have said that the motion of the heart was as perplexing as the flux and reflux of Euripus had appeared to Aristotle. At length, and by using greater and daily diligence, and collating numerous observations, I thought that I had attained the truth, that I should extricate myself and escape from this labyrinth, and that I had discovered, what I so much desired, both the motion and use of the heart and the arteries. Since which time I have not hesitated to expose my views upon this subject, not only in private to my friends, but also in public, in my anatomical lectures, after the manner of the Academy of old."

From a Biographical Sketch of Harvey in the Philosophical Transactions, London, Abridgment, 1809, p. 319.

"He shows, by experiments made on living animals, that the motion of the heart is performed by the contraction of its muscular fibres; that the auricles contract first, and thereby propel the blood into the ventricles; then the ventricles contract, whereby the blood is driven into the arteries; being prevented from returning into the auricles by the situation and connection of the valves. Now as by repeated contraction of the ventricles more blood is constantly propelled into the arteries than can be supplied by nourishment thrown into the veins (as appears upon calculation), and as moreover the arteries cannot receive blood through any other channel but the veins; it follows either that the veins must be quickly emptied, and the arteries on the contrary every moment more and more distended, which however is not the case; or that the blood must flow back again from the arteries into the veins, by certain secret passages, or by pores of the flesh, or by mutual anastomoses of the arteries and veins. He demonstrated that the last mentioned communication takes place in the lungs. Again: as along the course of the arteries more blood is sent from the heart to all parts of the body than is necessary

for the nourishment of those parts, he infers that the superfluous blood is returned by the veins (that they may not be left empty) from the fact, that no blood is found in the veins if the great artery be tied. On the other hand if a ligature be placed on the vena cava at the place where it joins the right auricle, it will immediately become distended in a very surprising manner. Moreover it must be evident to every one (he observes) who considers the situation and connection of the valves, that the blood passes from the smaller branches of the veins into their trunks, and from thence to the heart."

(6)

M. Malpighi. Opera Omnia. Lugduni Batavarum. Apud Petrum Vander Aa Bibliopolam MDCLXXXVII, Vol. II. De Pulmnibus Epistola II, p. 328.

"These things being apparent as regards the mere structure and connection [of the lungs], microscopic observation discovers still more wonderful things. For if the heart is still pulsating, the contrary motion of the blood is to be observed in the vessels, although with difficulty, so that the circulation of the blood is plainly to be detected, and can be made out even more successfully in the mesentery and in the other large veins contained in the abdomen. The blood then [entering] an [air] cell by the impulse through the arteries, as one or another conspicuous branch passes by or ends in a cell, rains down, finely broken up, as though poured out, and, thus multitudinously divided, loses its ruddy color, and, carried sinuously about, is scattered on all sides until it lands at the walls and angles [of the air-cells] and the branches of the veins which take it up again.

"Nothing more could be seen in the living animal operated upon. Hence I had believed that the body of the blood broke out into an empty space, and was gathered together again by anf open-mouthed vessel and by the help of the structure of the walls [of the air-cells]. The basis for this view was offered by the tortuous movement of the blood, diffused as it was in various directions, and by the gathering of it together at a definite point; nevertheless, my faith was shaken by the [appearance of the] dried lung of a frog, which, as it happened, had retained the redness of the blood in its smallest parts (vessels as I found them afterward); for by the aid of a more perfect glass there appeared to the eye no longer points which looked like the skin called *Shagreen*, but in place of them, minute vessels mingled together ring-fashion, and so great is the divarication of these vessels, as they spring here from vein and they from artery, that there is no longer any order preserved, but they appear as a net-work made up of the prolongations of the two [main] vessels. This net-work not only occupies the entire area [of the air cell]; but extends to the walls and blends with the efferent vessel, as I was able to observe repeatedly, although with great difficulty, in the oblong lung of the tortoise, which is likewise membranous and diaphanous. Hence it was made apparent to the senses that the blood was divided up and flowed through tortuous vessels, and was not poured out into spaces, but moved always through little tubes and was scattered owing to the multitudinous bends of the vessel. Nor is it any new thing in nature for the terminal mouths of vessels to be joined together, since in the intestines or other parts the same plan is followed, and, even more wonderful though it may seem, the upper ends of veins are joined with the lower ends [of others] by anastomosis, as was very well observed by the most learned Fallopius.

"In order, however, to obtain and verify the foregoing results, tie the turgid lung with a string, at its junction with the heart, as it protrudes from an opened frog, and while it is every where abundantly flushed with blood; for such a lung when dried will continue to have its vessels swollen with blood, which then you will see exceedingly well by examining them against a horizontal sun with a microscope of a single lens. Or you may use another method in looking at the vessels. Place the lung upon a plate of crystal illuminated by the light of a lantern from beneath through a tube: employ for this a microscope of two lenses, and there will be visible to you vessels arranged in rings, and by means of the same disposition of instruments and light you will observe the movement of the blood through the said vessels; and, by varying the amount of light, you will be able to contrive for yourself other things which defy description by the pen.

(7 and 8)

Account of some Discoveries made by Mr. Galvani, of Bologna; with Experiments and Observations on them. In two letters from Mr. Alexander Volta, F. R. S. Professor of Natural Philosophy in the University of Pavia, to Mr. Tiberius Cavello, F. R. S. Read Jan. 31st, 1793. Philosophical Transactions, London, 1793, pp. 10–44.

The fact that these letters are written in Old and very bad French renders a certain freedom of translation necessary.

In speaking of the Commentary of Galvani, entitled "ALOYSII BONONIÆ GALVANI *de Viribus Electricitatis in Motu Musclari Commentarius,* 1791, 4to; de 58 pages, avec quatere grandes planches," Volta says "it contains one of the most beautiful and surprising discoveries, and the germ of many others.

(1) "Dr. Galvani, having dissected and prepared a frog in such a manner that the legs were attached to the spinal cord only by the exposed crural nerves, and having cut off the rest of the body, saw that he excited lively movements in the legs, with spasmodic contraction of all the muscles, each time that a spark was drawn from the conductor, not only on the body of the animal, but upon every other body, and in every direction (the legs being at a considerable distance from the large conductor of the electrical machine, and under certain other circumstances which I shall explain further on).

"The required circumstances were, therefore, that the animal thus dissected should be in contact or very near some sort of metal or other good conductor, sufficiently extended, and better yet, between two similar conductors, one of which should be turned to the extremity of said legs, or some one of their muscles, the other toward the spine or the nerves: it was also very advantageous that one of these conductors (which the author distinguished by the names of *nerve-conductor* and *muscle-conductor*) and preferably the latter, be in free communication with the floor. It is in this position, especially, that the legs of the frog, prepared as has been described, received violent shocks, and twitched and struggled with vivacity at each spark of the conductor from the machine, although it was quite far distant, and although the discharge was made neither on the nerve-conductor nor on the muscle-conductor, but on any other equally distant from them, having all communication for the transmission of such a discharge, for example, on a person placed in the opposite corner of the room."

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(5) "I applied myself with considerable attention to determine what was the least electric force necessary to produce these results in the frog intact and full of life, as well as one dissected and prepared in the manner described; which Mr. Galvani had omitted to do. I chose the frog in preference to any other animal because it is endowed with great vitality and is easily prepared. Moreover, I have made experiments upon other small animals, with the same end in view, and with about an equal success. To properly estimate the value of the electric force, I thought it proper to subject the animal, destined for experiments of this kind, not to the return currents occasioned by the atmosphere, but to the direct electric discharges, now by a simple conductor, now by a Leyden jar, in such a manner that all the current should go through the body of the animal. To this effect I was careful to hold it isolated in some manner or other, and more often by fastening it with pins to two plates of soft wood, supported by glass columns."

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(8) "Thus we have, in the legs of the frog attached to the spinal column solely by the uncovered nerves, a new kind of electrometer; since electric discharges which give no indications with the ordinary machines, give marked signs with such an *animal electrometer*."

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(11) "Mr. Galvani did not stop here in these truly astonishing experiments on the frog; he extended them with success not only to other cold blooded animals but to birds; in which he obtained the same results by means of the same preparations; which consisted in disengaging one of the principal nerves from its envelope, where it entered a member susceptible of movement, arming such a nerve with a piece of metal, and establishing a communication, by means of a conducting arc, of the nerve and its muscles" [with the machine].

(12) "He also very happily discovered, and demonstrated in a very evident manner, the existence of an *animal electricity* in all or nearly all animals."

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(19) "Experiment A. I caught with forceps the ischiatic nerve a little below its insertion in the thigh, and applied wires, a piece of money or other metallic plate, a little higher up upon the same nerve, carefully dissected from its attachments, and held up by a thread, or supported by a plate of glass, a stick of "bees' wax, or of dry wood, or any other poor conductor. Then applying the body of a Leyden jar, very feebly charged, to said forceps, I carried the arc into contact with the other metallic plate, and saw that the discharge was made; which, though not strong enough to give the least spark, caused all the muscles of the thigh and leg to become convulsed and twitch more or less impetuously. This was true of the nerve throughout the entire leg, or any part of the nerve projecting beyond it, when in the course pursued by the current in its transit; though but a small portion of the nerve be irritated, this nevertheless, was sufficient to occasion contraction of the muscles."

(9)

An Account of an Experiment, made by Mr. Hook, of preserving Animals alive by blowing into their Lungs with Bellows. Philosophical Transactions, London, No. 28, p. 539.

"I did, therefore, heretofore give this Illustrious Society an account of an

experiment I formerly tried of keeping a dog alive after his thorax was all displayed by the cutting away of the ribs and diaphragm, and after the pericardium of the heart was also taken off. But divers persons seeming to doubt of the certainty of the experiment (by reason that some trials of this matter, made by some other hands, failed of success), I caused at the last meeting the same experiment to be shown in the presence of this Noble Company, and that with the same success as it had been made by me at first, the dog being kept alive by the reciprocal blowing up of his lungs with bellows, and then suffered to subside, for the space of an hour or more after his thorax had been displayed and his aspera arteria (trachea) cut off just below the epiglottis, and bound upon the nose of the bellows."

(10)

The Croonian Lecture on some Physiological Researches, respecting the Influence of the Brain on the Action of the Heart, and on the Generation of animal Heat. By Mr. B. C. Brodie, F.R.S. Read Dec. 20th, 1810. Philosophical Transactions, London, 1811, vol. xi, p. 36.

"In making experiments on animals to ascertain how far the influence of the brain is necessary to the action of the heart, I found that when an animal was pithed by dividing the spinal marrow in the upper part of the neck, respiration was immediately destroyed, but the heart still continued to contract, circulating dark colored blood, and that in some instances from 10–15 minutes elapsed before its action had entirely ceased. I further found that when the head was removed, the divided blood-vessels being secured by a ligature, the circulation still continued, apparently unaffected by the entire absence of the brain. These experiments confirmed the observations of Mr. Cruikshank (Phil. Trans. 1795) and M. Bichat (Récherches Physiologiques sur la Vie et la Mort) that the brain is not directly necessary to the heart, and that when the functions of the brain are destroyed, the circulation ceases only in consequence of the suspension of the respiration. This led me to conclude, that, if respiration were produced artificially, the heart would continue to contract for a still longer period of time after the removal of the brain. The truth of this conclusion was ascertained by the following experiment.

"Experiment 8.—I divided the spinal marrow of a rabbit in the space between the occiput and the atlas, and having made an opening into the trachea, fitted into it a tube of elastic gum, to which was connected a small pair of bellows, so constructed that the lungs might be inflated, and then allowed to empty themselves. By repeating this process once in five seconds, the lungs being each time fully inflated with fresh atmospheric air, an artificial respiration was kept up. I then secured the blood vessels in the neck, and removed the head, by cutting through the soft parts above the ligature, and separating the occiput from the atlas. The heart continued to contract, apparently with as much strength and frequency as in the living animal. I examined the blood in the different sets of vessels, and found it dark colored in the venæ cavæ and pulmonary artery, and of the usual florid red color in the pulmonary veins and aorta. At the end of 25 minutes from the time of the spinal marrow being divided, the action of the heart became fainter, and the experiment was put an end to."

(11)

New Pneumatic Experiments about Respiration, by the Hon. Robert Boyle. Phil. Trans. Lond. No. 62, p. 2011.

The account of these experiments is so long that it will be impossible to reproduce it here. The headings or "Titles" of the different chapters will give a sufficient insight into the experiments themselves. The air-pump, then newly invented, was employed in nearly all of them.

"THE FIRST TITLE.

Observations on the lasting of Ducks included in the Exhausted Receiver.

THE SECOND TITLE.

Of the Phænomena afforded by Vipers in an Exhausted Receiver.

THE THIRD TITLE.

Of the Phænomena afforded by Frogs in an Exhausted Receiver.

THE FOURTH TITLE.

Of the Phænomena afforded by a newly kittened Kitling in the Exhausted Receiver.

THE FIFTH TITLE.

Some Trials about Air usually harbored and concealed in the Pores of the Water, &c.

THE SIXTH TITLE.

Of the Phænomena afforded by Shell Fishes in an Exhausted Receiver.

THE SEVENTH TITLE.

Of the Phænomena of a Scale Fish in an Exhausted Receiver.

THE EIGHTH TITLE.

Of two Animals with large Wounds in the Abdomen, included in the Pneumatic Receiver.

THE NINTH TITLE.

Of the Motion of the separated Heart of a Cold Animal in the Exhausted Receiver.

THE TENTH TITLE.

A Comparison of the Times wherein Animals may be killed by Drowning, or withdrawing of the Air.

THE ELEVENTH TITLE.

Of Accidents that happened to Animals in Air brought to a considerable degree, but not near the utmost of Rarefaction.

A digressive Experiment concerning Respiration upon very high Mountains.

THE TWELFTH TITLE.

Of the Observations produced in an Animal in Changes as to Rarity and Density made in the self-same Air.

THE THIRTEENTH TITLE.

Of an unsuccessful Attempt to prevent the Necessity of Respiration by the Production or Growth of Animals in our Vacuum.

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THE FIFTEENTH TITLE.

Some Experiments, showing that Air, become unfit for Respiration, may retain its wonted Pressure.

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THE SEVENTEENTH TITLE.

Of the long Continuance of a Slow-worm and a Leech alive in the Vacuum made by our Engine.

THE EIGHTEENTH TITLE.

Of what happened to some Creeping Insects in our Vacuum.

THE NINETEENTH TITLE.

Of Phænomena suggested by Winged Insects in our Vacuum.

THE TWENTIETH TITLE.

Of the Necessity of Air to the Motion of such small Creatures as Ants, and even Mites themselves."

(12)

Joseph Priestley's Experiments on Respiration. Philosophical Transactions, London. Vol. lxii, p. 147. Read March 5th, 12th, 19th, 26th, 1772.

His first experiments were upon "fixed air" (carbon dioxide), and for the purpose he used "insects and animals which breathe very little" and frogs.

He then tried different methods for restoring air, in which candles had been burned, to its former state, such as the effects of heat, cold, and condensation.

p. 166. "Though this experiment failed, I flatter myself that I have accidentally hit upon a method of restoring air which has been injured by the burning of candles, and that I have discovered at least one of the restoratives which nature employs for this purpose. It is vegetation."

"On the 17th of August, 1771, I put a sprig of mint into a quantity of air, in which a wax candle had burned out, and found that on the 27th of the same month, another candle burned perfectly well in it."

"This restoration of air I found depended upon the vegetating state of the plant; for though I kept a great number of the fresh leaves of mint in a small quantity of air in which a candle had burned out, and changed them frequently, for a long space of time, I could perceive no melioration in the state of the air."

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p. 181. "That candles will burn only a certain time, is a fact not better known, than it is that animals can live only a certain time, in a given quantity of air; but the cause of the death of the animal is not better known than that of the extinction of flame in the same circumstances."

Priestley noticed that plants, put into air tainted by putrefaction, grew vigorously, and at page 193 he says, "This observation led me to conclude, that plants, instead of affecting the air in the same manner with animal respiration, reverse the effect of breathing, and tend to keep the atmosphere sweet and wholesome, when it is become noxious, in consequence of animals living and breathing, or dying and putrefying, in it."

He fully proved his conclusion by experiments upon mice, and the experiments will be found in detail in the article from which I have quoted.

(13)

Traité Élémentaire de Chimie par Lavoisier. 3d. ed. 1801 t. ii, p. 173.

Expériences sur la Respiration des Animaux, et sur les Changemens qui arrivent à l' air en passant par leur poumon.

"I confined in a convenient apparatus, of which it will be difficult to give an idea without recourse to figures, 50 cubic inches of common air: I introduced into this apparatus 4 ounces of very pure mercury, and proceeded to the calcination of it by keeping up for twelve days a degree of heat almost equal to that which is necessary to make it boil.

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I observed that the air which the vessel contained was diminished by 8 or 9 cubic inches.

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This air thus diminished, would not precipitate lime water, but it extinguished flames, and caused animals placed in it to perish in a little while.

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In the preceding experiment, the mercury in calcining had absorbed the better part, the respirable part of the air, and had left the mephitic or non-respirable."

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By reduction he "re-established the air to almost exactly the state it had before calcination, that is to say, the state of common air. This air thus re-established, no longer extinguished flames, no longer killed animals which breathed it.

"Here then is an example of the very complete proof at which one can arrive by means of chemistry, the decomposition of the air and its recomposition; it evidently results:

First, that five-sixths of the air which we breathe is, as I have already announced in a preceding Memoir, in a mephitic state, that is to say, incapable of maintaining the respiration of animals, and the combustion of bodies.

Second, that the surplus, that is to say, one-sixth only of the volume of atmospheric air is respirable.

Third, that in the calcination of mercury, this metallic substance absorbs the healthful part of the air leaving only the mephitic.

Fourth, that in bringing these two parts of the air, thus separated, together, the respirable part and the mephitic part, one makes again air like that of the atmosphere."

(14)

An account of the Method of conveying Liquors immediately into the Mass of the Blood. By Mr. Oldenburg. Philosophical Transactions, London. No. 7, p. 128 (Abridgment, vol. i, p. 45).

"In this account it is asserted that the discovery of a method of conveying liquor immediately into the mass of the blood is due to Dr. Christopher Wren, at that time Savillian professor in the University of Oxford. The method which he followed was to make a ligature on the veins and having made an opening into them on the side of the ligature towards the heart, to introduce into them slender syringes or quills fastened to bladders (in the manner of clyster pipes) containing the matter to be injected; performing the operation upon pretty big and lean dogs, that the vessels might be large enough and

easily accessible. These experiments were made at different times upon several dogs. Opium and the infusion of crocus metallorum were injected into the veins of the hind legs of these animals. The opium soon stupefied, though did not kill the dog; but a large dose of crocus metallorum induced vomiting and death in another dog. These experiments are more circumstantially related by Mr. Boyle, in his excellent book on the "Usefulness of Experimental Philosophy, Part II, Essay II, pp. 53–55."

A Letter from Dr. Timothy Clark. Phil. Trans. Lond. No. 35, p. 672,

Dr. Clark here gives the time of the infusing of liquors into the blood by Dr. Christopher Wren, showing that it was done in the house of the French ambassador, Duc de Bordeaux, in the year 1657.

In a letter from Dr. Timothy Clark in the Philosophical Transactions, No. 35,
(15)
p. 672, it is stated that Dr. Richard Lower was the first who performed trans-
(16)
fusion on brutes, and that the French anatomist, Dr. Denis, was the first who tried it on man; that the account of Dr. Lower's experiment was published in the Phil. Trans. for Dec. 1666, but nothing was heard of Dr. Denis' operation until March 1667.

Richard Lower and Dr. King appear to have been the first who performed the experiment of transfusion of blood. The account will be found in *De Corde, item de motu et colore Sanguinis et Chyli in eo transitu*, 1669.

(17)

"The Method observed in Transfusing the Blood out of one Animal into another. By the Hon. Robert Boyle.

Phil. Trans. Lond. No. 20, p. 353. (Abridgment, 1809, vol. i, p. 128).

"The method here described was first practised by D. Lower of Oxford.

Take the carotid artery of the dog or other animal, whose blood is to be transfused into another of the same or a different kind, and separate it from the nerve of the eighth pair, and lay it bare above an inch. Then make a strong ligature on the upper part of the artery not to be untied again; but an inch below, viz: towards the heart, make another ligature of a running knot, which may be loosened or fastened as there shall be occasion. Having made these two knots, draw two threads under the artery between the two ligatures; and then open the artery and put in a quill, and tie the artery upon the quill very fast by those two threads, and stop the quill with a stick. After this make bare the jugular vein in the other dog about an inch and a half long; and at each end make a ligature with a running knot, and in the space betwixt the two running knots, draw under the vein two threads as in the other; then make an incision in the vein, and put into it two quills, one into the descendant part of the vein, to receive the blood from the other dog, and carry it to the heart; and the other quill put into the other part of the jugular vein, which comes from the head (out of which the second dog's own blood must run into the dishes).

"These two quills being put in and tied fast, stop them with a stick till there be occasion to open them. All things being thus prepared, tie the dogs on their sides towards one another so conveniently that the quills may go into

each other, (for the dogs' necks cannot be brought so near, but that you must put two or three several quills more into the first two to convey the blood from one to another). After that unstop the quill that goes down into the first dog's jugular vein, and the other quill coming out of the other dog's artery; and by the help of two or three other quills put into each other, according as there shall be occasion, insert them into one another. Then slip the running knots and immediately the blood runs through the quills as through an artery, very impetuously. And immediately as the blood runs into the other dog, unstop the other quill coming out of the upper part of the jugular vein (a ligature being first made about his neck, or else his other jugular vein being compressed by one's finger); and let his own blood run out at the same time into dishes, (yet not too constantly, but according as you perceive him able to bear it) till the other dog begins to cry and faint, and fall into convulsions, and at last die by his side.

Then take out both quills out of the dog's jugular vein, and tie the running knot fast, and cut the vein asunder, (which you may do without any harm to the dog, one jugular vein being sufficient to convey all the blood from the head and upper parts, by reason of a large *anastomosis*, whereby both jugular veins meet about the *larynx*). This done, sew up the skin and dismiss him, and the dog will leap from the table and shake himself and run away, as if nothing ailed him."

(18)

Sir Charles Bell. Nervous System of the Human Body. Third Edition, London, 1844.

Page 24. "It was necessary to know, in the first place, whether the phenomena exhibited on injuring the separate roots of the spinal nerves corresponded with what was suggested by their anatomy. After refraining long, on account of the unpleasant nature of the operation, I at last opened the spinal canal of a rabbit, and cut the posterior roots of the nerves of the lower extremity; the creature still crawled, and there was no convulsion of the muscles of the back, but on touching the anterior fasciculus with the point of the knife, the muscles of the back were immediately convulsed."

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Page 25. "Every touch of the probe, or needle, on the threads of this root, was attended with a muscular motion as distinct as the motion produced by touching the keys of a harpsichord. These experiments satisfied me that the different roots, and different columns from which those roots arose, were appropriated to different offices, and that the notions derived from anatomy were correct."

Page 26. "On finding this confirmation of the opinion that the anterior column of the spinal marrow and the anterior roots of the spinal nerves were for motion, the inference presented itself that the posterior roots were for sensibility. But here a difficulty arose. An opinion prevailed that ganglions were intended to cut off sensation; and every one of those nerves, which I supposed were the instruments of sensation, have ganglions on their roots.

Some very decided experiment was necessary to overturn this dogma. I selected two nerves of the encephalon; the fifth which had a ganglion, and the seventh which had no ganglion. On cutting across the nerve of the fifth pair on the face of an ass, it was found that the sensibility of the parts to

which it was distributed was entirely destroyed. On cutting across the nerve of the seventh pair on the side of the face of an ass, the sensibility was not in the slightest degree diminished.

By pursuing this inquiry, I found that the sole organ of sensation in the head and face is a ganglionic nerve. Ganglions were therefore no hindrance to sensation, but on the contrary, a necessary accompaniment to a nerve of sensibility ; and thus my opinion was confirmed, that the ganglionic roots of the spinal nerves were the fasces or faciciculi for sensation.

Page 28. The nerve of the fifth pair was exposed at its root, in an ass, the moment the animal was killed ; and on irritating the nerve, the muscles of the jaw acted, and closed with a snap. On dividing the root of the nerve in a living animal, the jaw fell relaxed. Thus its functions were no longer a matter of doubt: it was proved to be at once a muscular nerve and a nerve of sensibility. And thus the opinion was confirmed, that the fifth nerve is to the head what the spinal nerves are to the other parts of the body, in respect to sensation and volition."

(19)

Magendie. Expériences sur les fonctions des racines des nerfs rachidiens. Jour. de Phys. 1822, p. 276.

"A second, a third experiment gave me exactly the same result; I commenced to regard it as probable that the posterior roots of the spinal nerves could well have functions different from the anterior roots, and that they were more particularly destined for sensibility."

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p. 279. "I have repeated and varied these experiments upon several species of animals : the results which I am about to announce have been confirmed in the most complete manner, be it for the anterior members, or for the posterior. I shall pursue these researches and give a more detailed account of them in a future number. It is suficient for me to be able to announce to-day as positive that the anterior and the posterior roots of the nerves which take origin from the spinal cord have different functions, that the posterior seem more particularly detined for sensibility, while the anterior seem more especially connected with movement."

(20)

L'Œuvre de Claude Bernard. Paris. Baillière. Leçons de Physiologie ; Substances Toxiques.

Système Nerveux. Recurrent sensibility, Vol. I. pp. 25-112.

Discovery of function of sympathetic in the neck, pp. 317-327.

Page 320. "However, the phenomena following seetion of the cervical branch of the great sympathetic are not limited only to the pupil. I have found that at the same time there is acceleration of the circulation in all the corresponding half of the head, the temperature of which rises ; the skin becomes more sensitive ; and, the arterial pulsation is stronger on this side, and the vessels are dilated."

For Bernard's work on the action of digitalis see

Action physiologique de la digitale et de la digitaline.

Gourvat, 4°, 74 pp., 1870.

(21)

Brodie, B. C. Experiments and Observations on the different Modes in which Death is produced by certain vegetable Poisons. Communicated by the Society for promoting the knowlege of Animal Chemistry. Read Feb. 21st, 1811. Philosophical Transactions, London, 1811, vol. xi, p. 178.

(22)

On the Reflex Function of the Medulla Oblongata and Medulla Spinalis. By Marshall Hall, M.D., F.R.S.L. and E. etc. etc. Read June 20, 1833. Philosophical Transactions 1833. p. 644.

"The first experiment which I made was upon the turtle. The animal was decapitated in the manner usual with cooks, by means of a knife, which divided the second or third vertebra.

"The head being placed upon the table for observation, it was first remarked that the mouth opened and shut, and that the submaxillary integument descended and ascended, alternately, from time to time, replacing the acts of respiration. I now touched the eye or eye-lid with the probe. It was immediately closed : the other eye closed simultaneously. I then touched the nostril with the probe. The mouth was immediately opened widely, and the submaxillary membrane distended. This effect was especially induced on touching the nasal fringes situated just within the anterior part of the maxilla. I passed the probe up the trachea and touched the larynx. This was immediately followed by a forcible convulsive contraction of the muscles annexed to it. Having made and repeated these observations, I gently withdrew the medulla and brain. All the phenomena ceased from that moment. The eye, the nostril, and larynx were stimulated, but no movement followed.

"The next observations were made upon the other parts of the animal. The limbs, the tail, were stimulated by a pointed instrument or a lighted taper. They were immediately moved with rapidity. The sphincter was perfectly circular and closed ; it was contracted still more forcibly on the application of the stimulus. The limbs and tail possessed a certain degree of firmness or tone, recoiled on being drawn from their position, and moved with energy on the application of a stimulus. On withdrawing the spinal marrow gently out of its canal, all these phenomena ceased. The limbs were no longer obedient to stimuli, and became perfectly flaccid, having lost all their resilience. The sphincter lost its circular form and its contracted state, becoming lax, flaccid, and shapeless. The tail was flaccid, and unmoved on the application of stimuli.

"These experiments afford evidence of many important facts in physiology. It proves that the presence of the medulla oblongata and spinalis is necessary to the contractile function of the eyelids, the submaxillary textures, the larynx, the sphincters, the limbs, the tail, on the application of the stimuli to the cutaneous surfaces of mucus membranes. It proves the reflex character of this property of the medulla oblongata and spinalis, and the dependence of these motions upon the reflex function. It proves that the tone of the limbs, and the contractile property of the sphincter, depend upon the same reflex function of the medulla spinalis—effects not hitherto suspected by physiologists.

"On another occasion, having removed the head of a frog, I divided the spine between the 3rd and 4th vertebra, and separated the upper portion of the animal from the lower. There were then the head, the anterior extremity,

and posterior extremity, with their corresponding portions of medulla, as three distinct parts of the animal. Each preserved the reflex function. On touching the eye, it was retracted, and the eyelids closed, whilst similar phenomena were observed simultaneously in the other eye. On removing the medulla, these phenomena ceased. On touching the toe of one of the anterior extremities, the limb and the opposite limb equally moved. On removing the spinal marrow, this phenomenon also ceased. Precisely similar efforts were observed in regard to the posterior extremity.

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"One of the most remarkable of the phenomena attached to the reflex function in animals, is that presented by those muscles of the hedgehog (Erinaceus Europaeus) by means of which that animal assumes, in certain circumstances, the form and firmness of a ball. The reflex function seems specially to connect the roots of the spine with the muscles. If the animal be examined under the influence of hybernation, the reflex function continues for some hours after the brain has been removed: the panniculus carnosus, the limbs, the tail, the larynx, the sphincter ani, remain excitable, and retain a degree of tone. These phenomena cease on removing the medulla spinalis.

"In the case of the decapitated young hedgehog, after all gasping had ceased, motions of the larynx are still excited on irritating the nostrils, or on irritating the medulla itself; just as the peculiar motions of the trunk are excited on irritating the limbs, tail or spines,—or the spinal marrow.

"Nor are we without evidence that the same principles obtain in the human subject. The condition of the infant born without cerebrum or cerebellum, and breathing from the influence of the medulla oblongata alone, is precisely that of the reflex function, with the addition of respiration. Such a case has been witnessed and described by Lawrence. 'The child moved briskly at first, but remained quiet afterwards, except when the tumor was pressed, which occasioned general convulsions. It breathed naturally, and was not observed to be deficient in warmth, until its powers declined. I regret that from fear of alarming the mother, no attempt was made to see whether it would take the breast: a little food was given it by the hand. It voided urine twice the first day, and once a day afterwards; it had three dark colored evacuations. The medulla spinalis was continued for about an inch above the foramen magnum, swelling out into a small bulb, which formed the soft tumor on the base of the skull. All the nerves from the fifth to the ninth were connected to this.' This brief detail is full of interest. The respiration was natural, the medulla oblongata being entire. Swallowing was affected when food was brought into contact with the pharynx; the sphincters performed their functions; the limbs were moved when the skin was first impressed by atmospheric air. There was no indication of sensation—the child remained quiet after the first brisk movements; and no event is mentioned which could establish the existence of voluntary motion,—the acts of swallowing, and of the expulsion of the urine and faeces, with the functions of the larynx and of the sphincters, belong distinctly to the excito-motory system."

(23)

Œuvres de Legallois avec des notes de M. Pariset. Paris 1824, t. I, p. 64.

"Respiration does not depend upon the whole brain, but upon a quite circumscribed part of the medulla oblongata, which is situated at a little dis-

tance from the occipital foramen and toward the origin of the nerves of the eighth pair (or pneumogastrics). For if one opens the cranium of a young rabbit, and extracts the brain by successive portions, from before backward, by cutting slices, one can remove in this manner all of the brain so-called, and afterward all of the cerebellum and a portion of the medulla oblongata. But it (respiration) ceases suddenly when one comes to include in the section the origin of the nerves of the eighth pair."

(24)

Recherches Expérimentales sur les Propriétés et les Functions du Systènte Nerveux dans les Animaux Vertébrés par P. Flourens. Paris 1842, p. 55.

§ VI. "General Conclusions of the Chapter.

I. The results obtained upon reptiles and mammals reproduce then and confirm the results given by birds:

With destruction of the cerebral lobes coincides constantly loss of volition and perception;

With destruction of a single lobe, loss of vision in the opposite eye;

With the destruction of the cerebellum, loss [of the power] of jumping, flight, walking, standing, etc.;

With destruction of the medulla oblongata, of the spinal cord, of the nerves, [coincides] loss of muscular contraction, and, in consequence, loss of movement, and death.

II. Contractions, the immediate excitation of contractions, the association of these contractions in movements of the whole body, the coördination of these movements in jumping, flying, walking, or standing, etc., the willing of these movements, sensations, perceptions, all these phenomena are then independent; the organs from which they are derived, distinct; their isolation, manifest; their localization, demonstrated."

§ II.

Page 189. I.—We have seen in the preceding chapter that the medulla oblongata is, in all these classes [mammals, birds, frogs, reptiles, and fishes], the organ which is the prime mover or the chief *exciter* and *regulator* of the inspiratory movements; it is, moreover, in all these classes, the organ immediately productive, through the nerves, of the inspiratory movements, particularly of the face and head; lastly, it is, in fine, in fishes, as I shall show, the prime moving organ, and the organ immediately productive of *all* respiratory movements.

II.—The medulla oblongata is then, in all the classes, the essential and primordial organ of the respiratory mechanism; it is the exclusive organ of this mechanism in fishes."

(25)

An Account of Mr. Hunter's Method of Performing the Operation for the Cure of Popliteal Aneurism. Sir Everard Home, Bart. Works of John Hunter with Notes by J. F. Palmer, 4 vols. London, 1835. Vol. iii, p. 596.

"Mr. Hunter finding an alteration of structure in the coats of the artery previous to its dilation, and that the artery immediately above the sac seldom unites when tied up in the operation for aneurism, so that as soon as the ligature comes away, the secondary bleeding destroys the patient, was led to conclude that a previous disease took place in the coats of the artery, in conse-

quence of which it admitted of dilatation capable of producing an aneurism. But not satisfied with the experiments on frogs, given by Haller in support of the opinion that weakness alone was sufficient to produce the dilatation, he resolved to try the result in a quadruped, which, from the vessels being very similar in structure to those of the human subject, would be more likely to ascertain the truth or fallacy of Haller's opinion."

Mr. Hunter's account of the experiment: *Ibid.*, vol. i, p. 544.

"However, whatever may have been either the remote or immediate cause," [of aneurism] "it must, in fact, in all cases arise from a disproportion between the force of the blood and the strength of the artery, the coats being weakened so as not to be able to support the force of the blood in its passage along its canal, which therefore gives way. This weakness of the coats of the artery would appear, in most cases, to depend on disease, for accidents, *cœteris paribus*, have generally the power of recovery. As a proof of this, I will relate an experiment made to ascertain the truth of the existence of the mixed kind" [of aneurism], "which was supposed to arise from a partial destruction of the coats of an artery, and that the remaining coat being too weak to sustain the force of the circulation, gave way and distended. That the artery might have the full force of the blood's motion, I chose the carotid, as being near the heart.

One of the carotid arteries of a dog, for an inch in length, was laid bare, and its coat removed, layer after layer, until the blood was seen through the remaining transparent coat, and I had gone as far as I dared; I then left the artery alone for three weeks, when I killed the dog, expecting to find a dilatation of the artery as had been asserted; but to my surprise the sides of the wound had closed on the artery, and the whole was consolidated to and over it, forming a strong bond of union, so that the whole was stronger than ever."

Vol. III, p. 598. "Mr. Hunter, from having made these observations was led to propose that in this operation" [for popliteal aneurism] "the artery should be taken up in the anterior part of the thigh, at some distance from the diseased part, so as to diminish the risk of hemorrhage, and admit of the artery being more readily secured, should any such accident happen. The force of the circulation being thus taken off from the aneurismal sac, the progress of the disease would be stopped; and he thought it probable, that if the parts were left to themselves, the sac, with its contents, might be absorbed, and the whole of the tumor removed, which would render any opening into the sac unnecessary."

Experiments and Observations on the Growth of Bones, from the Papers of the Late Mr. Hunter. (Published by Mr. (afterwards Sir Everard) Home, in the Second Volume of the Transactions of a Society for the Improvement of Medical and Chirurgical Knowledge.) *Ibid.*, vol. iv, p. 315. Read October 4th, 1798.

"It was some time anterior to the year 1772 that Mr. Hunter began to investigate this subject, and an account of the experiments and observations was given to me to copy in that year, as a part of his future lectures.

Du Hamel had published a very ingenious theory upon the growth of bones, which he endeavored to support by experiments tending to prove that bones grow by the extension of their parts. With this doctrine Mr. Hunter was not satisfied, and instituted experiments to determine the truth of Du Hamel's opinion.

Mr. Hunter began his experiments by feeding animals with madder, which has the property of tinging with a red color that part only of the bone which is added while the animal is confined to this particular food. He fed two pigs with madder for a fortnight, and at the end of that period one of them was killed; the bones, upon examination externally, had a red appearance; when sections were made of them, the exterior part was found to be principally colored, and the interior was much less tinged.

The other pig was allowed to live for a fortnight longer, but had no madder in its food; it was then killed, and the exterior part of the bone was found of the natural color, but the interior was red.

He made many other experiments of the same kind upon the increase of the thickness of the neck and head of the thigh bone. From thence it appeared that the addition of new matter was made to the upper surface, and a proportional quantity of the old removed from the lower, so as to keep the neck of the same form, and relatively in its place.

To ascertain that the cylindrical bones are not elongated, by new matter being interposed in the interstices of the old, he made the following experiment: he bored two holes in the tibia of a pig, one near the upper end, and the other near the lower; the space between the holes was exactly two inches: a small leaden shot was inserted into each hole. When the bone had been increased in its length by the growth of the animal, the pig was killed, and the space within the two shot was also exactly two inches.

This experiment was repeated several times on different pigs, but the space between the two shot was never increased during the growth of the bone.

Besides these experiments on the growth of bones, he made others, to determine the process of their exfoliation.

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Bones, according to Mr. Hunter's doctrine, grow by two processes going on at the same time, and assisting each other; the arteries bring the supplies to the bone for its increase; the absorbents are at the same time employed in removing portions of the old bone, so as to give to the new the proper form. By these means the bone becomes larger, without having any material change produced in its external shape."

(26)

Experiments and Observations on the Union of Fractured Bones. By John Howship, Esq. Read March 17th, 1817. Medico-Chirurgical Transactions. London, 1818, vol, ix, p. 143.

Page 145. "The following experiments were made upon rabbits, selected at about the age of twelve months, the period at which, from their beginning to bear young, they may be considered to have nearly attained their full growth."

Six experiments were performed.

Page 170. "Having at length completed the account of my observations upon fracture, I shall now lay before the Society the conclusions drawn from the above enquiry, which will close the present paper.

The first effect of fracture is extravasation of blood into the surrounding soft parts, the quantity poured out varying according to the degree of contusion or complication."

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Page 171. "The blood effused in fracture suffers various degrees of change; but under all circumstances it forms the medium in which the ossific process is established."

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Page 172. "The mode of progress in the ossific process seems to indicate a degree of caution, as if a principal object was to guard against the possibility of the least disturbance or motion between the parts of the bone, subsequent to the act of union."

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"The circumstances of the fracture evidently regulate the quantity and seats of the ossific deposit. In simple transverse fracture with little contusion, where the bone is immediately reduced, and the limb kept perfectly quiet, the degree of internal laceration will be small, the effusion of blood inconsiderable, and the ultimate deposit of bone moderate in proportion."

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Page 173. "In oblique fracture, where the bones have suffered more violence at the moment of accident, and are retained with more difficulty when reduced, the effusion of blood will be greater, and the quantity of ossific matter formed will be also more abundant."

(27)

Flourens P. Récherches sur la formation des os. Compt. rend Acad. d. sc., Paris, 1844, xix, 621–625.

(28)

Heine, B. Ueber die Wiedererzeugung neuer Knochenmasse, und Bildung neuer Knochen. J. d. chir. u. Augenh. Berlin, 1836, xxiv, 513–527, also Gaz. Méd. de Paris, 1837, v, 386–388.

(29)

Syme. Trans. Roy. Soc. Edin., 1836, vol. xiv, p, 158.

(30)

Ollier, L. Des moyens chirurgicaux de favoriser la reproduction des os après les résections ; de la conservation du périoste ; résections sous-périostées ; de la conservation de la couche osseuse périphirique ; evidement des os.

Gaz. hebdom. de méd. Paris, 1858, v. 572, 651, 733, 769, 853, 899.

Ollier, L. Recherches experimentales sur la production artificielle des os, ou moyen de la transplantation due périoste et sur la régénération des os, aprés les résections et les ablations completes.

J. de la physiol. de l'homme, Par. 1859, ii, 1169, 468.

Ollier, L. De la transplantation des éléments anatomiques du blastème sous- périosteal ; formation des petites grains osseux dans la region où ont été semés ces éléments.

Compt. rend. Soc. de biol., Par. 1860, 3 s., i, 108.

Ollier, L. Nouvelle démonstration de la régénération osseuse après les résections sous- périostées articulaires.

Bull. gen. de thérap. etc., Paris, 1870, lxxix, 258–261.

Du Périoste au Point de Vue Physiologique et Chirurgical, communication faite au congrès medical de Lyon le 28 September, 1864, par M. Ollier, chirur-

gien en chef de l'Hôtel—Dieu de Lyon. Gaz. hebdom. de mèd. Par. 1865, 2 s. ii, 82, 116, 152, 195.

"Proposition First. That the periosteum produces osseous tissue by a normal development, in the order of its proper anatomic elements. The deeper layer, composed of protoplasmic cells, possesses this property, and to this layer I have given the name osteogenic."

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"I first repeated the experiments of my predecessors, but in studying the role of the periosteum, with Du Hamel in fracture, or Heine and M. Flourens in resections, I have recognized that it was difficult to determine the part played by the divers elements of the bone in the act of reproduction."

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"I isolated the different tissues, I studied them separately, either in their normal situation, preserving the while their anatomic relations, or displacing and transplanting them into distant regions. I experimented with the periosteum, the marrow, cartilage, bone, and the adjacent tissues, muscles and tendons and I arrived at results which permit the setting forth of propositions which I believe sufficiently exact to prevent all controversy."

"I commenced with the periosteum, which I detached from the bone; I first dissected up a piece of this membrane, 5 or 6 cm. long, from the tibia of a rabbit, I rolled it around the limb amongst the muscles and under the skin, and I obtained bone, or rather, osseous prolongations of varied form. I produced bone in a circle, in a spiral, in a cross, etc. etc.; and finally I gave to the new bone any form I desired, and for this purpose I had but to fix the periosteum in a predetermined way: after from 20–25 days (in the rabbit, the cat, or the dog) I found new bone of the form of the periosteum, or to speak more correctly, I found the periosteum ossified.

This experiment semed to me fundamental, it furnished simple and irrefutable proof of the osteogenic property of the periosteum; and it answered the greater part of the objections which had been offered to the doctrine of Du Hamel, from the time of Haller to Bichat.

It proved that the periosteum produces bone of itself, independently of the neighboring tissues; and from a surgical point of view it promised new resources in autoplasty; it also showed us the manner in which ossification takes place in abnormal regions. But I did not stop at this first experiment which I saw was so signal. Being anxious to obtain results of surgical value, I modified it so as to make it still more convincing, and by means of it answered all objections that it was possible for me to foresee.

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After having detached and fixed my shred of periosteum among the muscles, I left it to live, or at least to form certain adhesions during three or four days; then, finding that it had become ossified, I detached from the bone 4 or 5 mm. of the entire depth of the periosteum, in a manner to interrupt all connection between the periosteum and bone. I established then that, in spite of this interruption, the periosteum continued to ossify, and that new bone, independently of the normal bone, was formed there.

But this did not yet satisfy me. To answer at once all possible objections, I conceived the idea of transplanting the periosteum into distant regions, immediately after its separation from the bone.

I transplanted it from the leg to the forehead or back, and I saw that this membrane carried with it everywhere its osteogenic property. Everywhere I engrafted the periosteum new bone was formed ; this was not an unformed mass of calcareous particles, but a bone formed of the characteristic elements of osseous tissue, hollowing itself out into spaces in its interior, and having after a certain time a veritable canal containing medullary substance, and surrounded by a compact layer."

(31)

Mr. Rand. "A new method for the treatment of neuralgia by sub-cutaneous injection, 1855.

(32)

John Hunter, *loc cit.*

(33)

A Treatise on the Process Employed by Nature in Suppressing Hemorrhage from Divided and Punctured Arteries. J. F. D. Jones. 8°, Lond. 1802.

I have been unable to find the above treatise, but the following account of the experiments is given by Travers, *loc cit.* p. 440.

"Jones ascertained, that the effusion of lymph from the wound inflicted by the ligature was sufficient, even if the ligature were removed upon the instant, to obstruct the artery. By including a loose thread along with the artery in the ligature, he readily withdrew the latter after the infliction of the wound. In one instance he succeeded with a single ligature, and in several instances with two, three or four, made at a small distance apart. The lymph effused was in proportion to the extent of the section, or if this was incomplete, the union was equally so. He was led to conclude that the complete circular section of the internal coat was indispensable to union, and the success which attended his experiments led him to conjecture, that in some surgical cases removing the ligature as soon as it was made would be an efficient operation. This suggestion, the value of which he left to be determined by future experiments was caught at with eagerness by his readers, and by many considered to be the essence of his publications."

In a foot note, the following quotation is given from Jones, p. 136.

"I leave the the fact (viz.—the complete obstruction of an artery consequent upon the momentary application of a ligature) for those who have opportunities of applying it in practice, when all the circumstances which determine its success or failure shall have been fully ascertained by further experiments on brutes."

(34)

Observations upon the Ligature of Arteries and the Causes of Secondary Hemorrhage. Benjamin Travers. Medico-Chirurgical Transactions, vol. iv, p. 435. Read October 26th, 1813.

Page 439. "It is curious to observe the revolution which has taken place within a few years in this branch of surgical practice, since experimental inquiry has furnished the true explanation of the principle upon which the ligature acts. Mr. Hunter and the surgeons who after him practised the operation for popliteal aneurism, were in the habit of applying the ligature with force only sufficient to bring the sides of the vessel in contact; and some

included an extraneous body, as a piece of cork or wood, or a roll of linen, to prevent the lesion of the artery in the act of tightening the ligature. The fear of cutting the coats of the artery was uppermost in the minds of all, and next to this, the fear of quickening the process of ulceration, and the casting off of the ligature."

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Page 443. "The original experiment of Jones, in whatever light we view it, is of unquestionable importance, and deserves to be highly appreciated. While its occasional failure demonstrates that the apposition of the cut surfaces is essential to the certain obliteration of the vessel, its occasional success establishes that, *coeteris paribus*, it cannot with this precaution fail of its intention." As a basis for the statements made in this paper, Travers performed five experiments upon the ligaturing of arteries, using the ass, dog, and horse.

In another paper on the same subject, which appears in vol. vi of the Transactions of the Medico-Chirurgical Society, p. 632, he records nineteen other experiments.

The first eight were undertaken "To ascertain the earliest period at which the ligature might be removed, and the artery wounded without hemorrhage."

Page 643. "The experiments next to be related, give the operation of the compressor, and were undertaken with a view to determine its merits as a surgical instrument, comparatively with the ligature. Professor Assalini of Milan, who lately visited this country, entertains a preference for the practice of compression in the operation for aneurism. He had employed it with success in three cases of popliteal aneurism."

Experiment XV.—"I wished to know the effect of leaving the compressor upon the vessel, and the time in which it was liberated by ulceration."

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Page 658. "In contemplating the removal of the ligature at a given time, it becomes essential to ascertain if this can be done with equal security when a branch is contiguous as when at a distance. With this view I made the following experiments." (Exp. XVI–XIX.)

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Page 662. "The practical application of the facts and deductions contained in this and my former Essay (Vol. IV) will probably be the subject of a future communication to the Society.

"It is however, in my judgment, a subject too important to be lightly disposed of; and it carries with it, in reference to surgical practice, a responsibility too serious to justify a rude and hurried trial of its merits."

(35)

On the Torsion of Arteries as a means of Arresting Hemorrhage, with Experiments by Thomas Bryant, F.R.C.S. Medico-Chirurgical Transactions, vol. li, p. 199 (1868).

Page 203. "I propose to relate seriatim the experiments I have made upon the dog, horse and human subject to test the value of torsion, and to observe the process by which the vessels so treated become permanently sealed."

* * * * * * * * *

"Experiment 1. February 4th, 1868.—I divided the left *femoral artery* of a dog just below Poupart's ligament, and twisted the cardiac end by 'free' tor-

sion *four* times, with success. During this time the distal end was held by forceps, and when these were removed hemorrhage occurred; the bleeding extremity was, however, seized by forceps and twisted *four* complete revolutions, all bleeding at once ceased, and by the seventh day the wound had united.

The dog was killed the 11th day after the operation."

* * * * * * * * *

"Experiment IV.—February 11th, 1868.—I cut down upon and divided the right *common carotid* artery of a dog. I applied 'free' torsion to the cardiac end, making three revolutions without success, and accordingly seized the vessel again and twisted it four times more. Hemorrhage was at once arrested. *Three* complete twists were then given to the distal end of the artery, and no bleeding followed.

On the second day the dog was quite well, he had taken his food as usual, and appeared in no way disturbed by the operation. On the following day the animal was destroyed.

It must be noticed that in this case, as in the second experiment, three rotations of the artery were not sufficient to arrest bleeding; four proved successful in both cases."

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"Experiment VII. March 17th, 1868.—I cut down upon and divided the left *common carotid* artery of a horse; applied two pairs of torsion forceps transversely to the vessel, and divided the artery midway between them, leaving an inch of artery on the distal side of each pair of forceps. With a third pair of torsion forceps, I then seized the extremity of the artery at its cardiac end, and twisted it *seven* complete revolutions. I then removed the instrument that fixed the vessel, and not a drop of blood escaped; the pulsations in the vessel were very strong. The same treatment was then applied to the distal end with a like result. It was certaiuly something astonishing to see the great vessel fill out and pulsate after the operation without one drop of blood escaping; and although the animal plunged somewhat during and after the operation, the success was must complete. The animal was allowed to live for forty-eight hours, and then killed."

(36)

Rayer and Davaine. Bull. de la Soc. de Biol. de Paris, 1850.

"In the blood are found little thread-like bodies about twice the length of a blood corpuscle. Those little bodies exhibit no spontaneous motion." However, no importance was attached to their presence.

Davaine. Nouvelles recherches sur les infusiores du sang dans la maladie connue sous le nom de sang de rate. Compt. rend. Soc. de Biol. 1863. Par. 1864, 3. s. v, 149–152.

(37)

The Life of the Trichina. (Monograph) 1864, p. 21. By Rudolph Virchow, M.D., Ph.D. Translated by Rufus King Brown, M.D.

The author states that he received from Dr. Zenker some of the muscle of a girl who died of trichinosis and also some of the flesh of the pig that caused her disease.

"A rabbit fed with the trichina from the girl, died in a month with its

flesh full of them. Some of its flesh was given to a second rabbit. It also died in a month. With this meat three other rabbits were fed. Of these, two died at the end of the third week, and the other in the fourth week. To another animal the meat of this was fed. As it ate but little it lived six weeks. In all these the muscles after death were found filled with trichina. Even in the smallest particle of their meat several were found."

(38)

Cause and Nature of Tuberculosis. J. A. Villemin. Gaz. hebdom. de méd. Par. 1865, 2. s., ii, 795.

"1. Tuberculosis is the effect of a specific agent, of a virus, in a word.

2. This agent should be found, as its congeners, in the morbid products which it gives rise to by a direct action upon the normal elements of the tissues affected.

3. Introduced into an organism susceptible to it, this agent should then reproduce itself, and reproduce, at the same time, the disease of which it is the essential and determining cause.

Experimentation is undertaken to confirm these inductive conclusions. The results are as follows :"—

1st Series. Of two rabbits, one is inoculated with two little fragments of tubercular tissue and pus from a lung cavity. The other is kept as a control. The two were placed under like conditions of existence. At the autopsies the inoculated rabbit was found to be infected, while its mate showed absolutely no sign of tubercle.

2d Series. Four rabbits were inoculated with tubercular matter, and, when killed, all of them were found infected. Two other rabbits which had been kept with these and afterward used for physiologic purposes presented no trace of tuberculization.

From these experiments, Villemin draws the following conclusions :—

"1. Pulmonary phthisis (as tubercular diseases in general) is a specific infection.

2. Its cause is an inoculable agent.

3. The inoculation can easily be made from man to the rabbit.

4. Tuberculosis belongs then to the class of virulent diseases, and should have a place, in the nosologic table, along with syphilis, but better, perhaps, with glanders and farcy."

Continuing his experiments to the 3d Series. three pairs of rabbits are taken, and one of each pair inoculated. Two of the pairs are put in the same cage. At the autopsies those not inoculated show no signs of tuberculosis.

(39)

De l'atténuation du virus du choléra des poules par M. L. Pasteur. Comptes Rendus, t. xci, p. 673.

Chamberland. Le Charbon et la Vaccination Charbonneuse d'après les travaux recents de M. Pasteur. (Paris, Tignol 1883), p. 9 *et seq.*

Translation for New Sydenham Society, 1886, p. 551 *et seq.*

"The experiments were commenced in the early days of August, 1878. They consisted at first in feeding certain lots of sheep with lucerne which had been watered with artificial cultivations of the bacterium of anthrax full of the parasite and its spores. * * * * Notwithanding the immense

number of the spores of the bacterium swallowed by all the sheep of each lot many of them, often after having been distinctly ill, escaped death ; a smaller number died with all the symptoms of spontaneous anthrax after a period of incubation which might extend to eight or ten days, although, at the end, the disease took on the almost sudden characters frequently noted by observers who have thus been led to believe in a very short period of incubation.

The mortality was increased by mixing with the food, sprinkled with the spores, sharp-pointed objects, especially the pointed extremities of the leaves of dried thistles, and above all the beards of ears of barley cut into small fragments about a millimeter long.

It was of great importance to ascertain whether the autopsy of animals dying under these conditions would show similar lesions to those observed in animals dying spontaneously in stables, or in flocks penned in the open air. The lesions in the two cases are identical, and their nature authorized the conclusion that the disease begins in the mouth or pharynx."

De l'atténuation des virus et de leur retour à la virulence, par M. L. Pasteur avec la collaboration de MM. Chamberland et Roux. Comptes Rendus, t. xcii. p. 429.

"I have made known in papers recently published the first example of the attention of a virus by experimental means alone. * * * * It seems probable that the oxygen of the air is the chief cause of these attenuations, that is to say, of these diminutions in the facility with which the microbe multiplies ; for it is clear that the various degrees of virulence are identified with the varying power of the parasite to develop in the economy. * * * * The virus of anthrax, being one of the best studied, must be the first to attract our attention. A mycelial growth of the bacterium entirely free from spores can be maintained in contact with pure air at a temperature between 42° C. and 43° C.

After an interval of about one month the cultivation is found to be dead, that is to say, fresh broth inoculated with it remains completely sterile. On the day before that on which this inability to grow is noted, and on every preceding day during the month, reproduction of the growth is, on the contrary, easy.

With regard to its virulence we discover this remarkable fact : after remaining for eight days at a temperature of 42° to 43° C., and ever afterwards the bacterium has lost its virulence ; at least its cultivations are inocuous to the guinea-pig, the rabbit, and the sheep, three of the animals most likely to contract splenic fever. We are, therefore, by using a simple artifice in cultivating, able to produce not merely an attenuation of virulence, but a suppression which is apparently complete. More than this, we have the power of preserving and cultivating the terrible microbe in this inoffensive condition.

Experimental application of the Method" [of inducing immunity].

"M. Pasteur proposed that 60 sheep should be used for this experiment, and consented, at the request of the President of the Agricultural Society, to extend the experiment to 10 cows. He foretold that all sheep not protected by inoculation of attenuated virus would die, and that all the cows not so protected would be, at least, made ill, and that some would die when inoculated with a very virulent virus ; while all the protected sheep would survive the inoculation with this very virulent virus, and that the cows would not be

made ill; 10 sheep were not to be dealt with in any way, but kept for ultimate comparison with the inoculated sheep."

For further work done by Pasteur on immunity consult

Sur la rage, par M. Pasteur avec la collaboration de MM. Chamberland et Roux. Comptes Rendus, t. xcviii, p. 1229, and

Méthode pour prevenir la rage après morsure, par M. L. Pasteur. Ibid., t. ci, p. 766.

(40)

The Etiology of Tuberculosis, by Dr. Robert Koch. Translated by Mr. Stanley Boyd in Microparasites in Disease, pp. 157–160. Infection Experiments with Tissue containing Tubercle Bacilli.

"The inoculation was effected by making a small incision in the abdominal wall of a guinea-pig with the scissors, inserting the point of the scissors to form a pocket-like subcutaneous wound about a half centimeter deep. Into this little pocket a fragment of the inoculation substance about the size of a millet-or mustard seed was pushed as deeply as possible. On the following day the inoculation wound was always united, glued together and showed no reaction. Generally it was not till after a couple of weeks that a visible swelling of the lymphatic glands next the seat of inoculation occurred, usually the inguinal glands on one side, and at the same time induration and the development of a nodule took place in the inoculated wound, which up till then had remained perfectly healed. After this the lymphatic glands enlarged rapidly, frequently to the size of a hazel-nut, the nodule at the seat of inoculation then generally broke and became covered with a dry crust, beneath which was a flat ulcer with a cheesy floor, discharging very slightly. The animals began to lose flesh about this time, their coat became bristly, dyspnœa set in, and they died generally between the fourth and eighth weeks, or they were killed within the same space of time. In some instances the inoculation substance was inserted into a pocket-like wound in the skin of a rabbit also. But as the course of the disease was not so constant and rapid as in the guinea-pigs after subcutaneous inoculation, I inoculated rabbits afterwards only in the anterior chamber of the eye.

The following inoculations were carried out in the way above described:—

1. Miliary tuberculosis. Tubercle of the pia mater, very rich in tubercle bacilli; 6 guina-pigs. Of these one died 5, two 6, and two 7 weeks after inoculation. The sixth was killed in the eighth week. In all the animals the lungs, liver and spleen were highly tubercular, and the inguinal glands had undergone caseation.

2. Miliary tuberculosis. Grey nodules in the lungs, with fairly numerous tubercle bacilli: 6 guinea-pigs. Three died in the sixth week; the rest were killed some days later. All tubercular, as in No. 1.

3. Miliary tuberculosis. Grayish yellow nodules from the spleen and kidneys, with not many tubercle bacilli: 6 guinea-pigs. Died in the 6th and 7th weeks. All tubercular, as in No. 1.

4. Miliary tuberculosis. Grey nodules from the lung, fairly rich in bacilli: 3 guinea-pigs. Two died in the 6th, one in the 7th week. All tubercular, as in No. 1.

5. Miliary tuberculosis. Grey nodules from the lung containing few bacilli: 5 guinea-pigs, 2 rabbits at the root of the ear. One guinea-pig died after 8

weeks, the remainder were killed some days later. All were tubercular. The rabbits killed after 10 weeks had caseous lymphatic glands at the root of the ear and in the neck, tolerably abundant grey nodules in the lungs, a few in the kidneys and the spleen. Five more guinea-pigs were inoculated with the tubercles from the spleen of one of the guinea-pigs. Three of these died in the 8th week. The two remaining were killed the same week, and all found tubercular. Some of the cheesy glandular substance from a rabbit was rubbed up with water and injected into the peritoneal cavity in two rabbits. When these two animals were killed after 8 weeks, tuberculosis of the omentum, spleen and liver was found, together with a fair number of gray nodules in both lungs.

6. Caseous pneumonia and tuberculosis of the meninges: 2 guinea-pigs inoculated with the cheesy substance from the lungs in which there were numbers of bacilli. The animals died in the 5th and 6th weeks. All tubercular.

7. Lungs showing caseous infiltration with many bacilli: 6 guina-pigs. The first died after 6 weeks, The remainder were very ill at the time and were killed a few days later. All tubercular.

8. Phthisical lungs with cavities, intestinal ulcers and cheesy mesenteric glands. Two guinea-pigs were inoculated from the contents of cavity containing a fair number of bacilli, and four more from the mesenteric glands, which were very full of bacilli. The latter died in the 5th and 6th weeks: of the first two, one died in the sixth week, and the other was killed a few days later. All tubercular.

9. Caseous bronchitis and intestinal tuberculosis. Five guinea-pigs were inoculated from the lung substance, in which there was a good number of bacilli. Two of them died in the 8th week. The remainder were killed before the end of the same week. All tubercular.

10. Phthisical lungs with cavities. Four guinea-pigs inoculated from the consolidated lung tissue, in which were only a few bacilli. Three of them died in the 7th and 8th weeks, the last not till the 12th week. All tubercular.

11. Phthisical sputum. Nine guinea-pigs were inoculated at different times with fresh sputum containing a varying number of tubercle bacilli taken from three different patients. Some of the animals died before the 8th week, some were then killed. They were all tubercular.

12. Phthisical sputum dried for 2 weeks: 3 guinea-pigs. Two died in the 6th week, the third was killed at the same time. All tubercular.

13. Phthisical sputum dried for two months: 3 guinea-pigs, killed after 5 weeks, and tubercles found in lungs, liver, and spleen.

14. Tuberculosis of the uterus and tubes. Six guinea-pigs inoculated with cheesy material from the tubes. Two animals died at 7 weeks. The others were killed in the 9th week. All tubercular.

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28. With lung tubercles from a second monkey, dying of spontaneous tuberculosis, 2 guinea-pigs were inoculated and died of tuberculosis in the 8th and 9th weeks. From these guinea-pigs again 2 guinea-pigs and 1 rabbit were inoculated. They were killed in the 6th week, as they seemed already ill, and they were found to be already tubercular.

Two more guinea-pigs were inoculated from the same monkey with lung tubercles which had been dried and kept for 3 days. They too were killed in the 6th week, and found tubercular.

For the infection experiments just detailed (including 13 not quoted) 79 guinea-pigs, 35 rabbits and 4 cats were used altogether, and the inoculation of these animals resulted in tuberculosis without exception."

(41 and 42)

Experiments on the Immunity and Cure of Tetanus in Animals. Zeitschr. f. Hygiene u. infections-Krankheiten, 12, 1892, 45–57. By Dr. Behring.

"In November, 1890, I, in an announcement with Mr. Kitasato, stated that with the blood of a rabbit rendered immune from tetanus, we could prevent mice from taking the disease, and if they had been infected we could cure them.

The certainty of the cure and the immunity of even such animals as had received more than a hundred times the dose of the fatal infection, exceeded our greatest expectation. If in the manipulation no technical mistakes were made, unfavorable results were entirely excluded."

Here the author states that the practicality of this method was suggested by his experiments in diphtheria, and that he and Dr. Kitasato arranged to do all they could to perfect the new method so it could be used for larger animals than mice, and especially that it might be used to render the human body immune from tetanus. They were stimulated to their research by the belief that they had a method which was applicable to different infectious diseases.

Drs. Kitasato and Behring carried on their investigations separately, but each assisted the other where possible.

The successful use of ICl_3 in diphtheria led Dr. Behring to apply it for the purpose of rendering immune from tetanus.

The author states that the experiments upon rabbits were very successful and that the experiments were among the easier tasks which a bacteriologist had to perform The first requisite of success being an exact knowledge of the action of the culture relatively to the filtrate. In one month Dr. Behring received 8 cultures from Dr. Kitasato and tested the effectiveness of them on mice and rabbits. He gives an account of the last of these cultures. It was received Nov. 15th, '91, in bouillon and had stood in the culture for ten days.

"Upon opening the paraffin the odor characteristic of tetanus was given off, and a microscopical examination revealed an abundance of bacteria and spores."

(43)

Archiv für Anatomie. 1870.

On the Electrical Irritability of the Cerebrum. By G. Fritsch and E. Hitzig.

Page 308. "In the first experiment we used unnarcotized animals, dogs, but later narcotized, and proceeded to open the skull in as level a spot as possible. Then with the sharp, round bone forceps we removed either the entire half of the skull, or only the part covering the frontal lobe of the brain.

In most cases after experimenting on one hemisphere, we removed the other half of the skull in exactly the same way. In all these cases, after one dog had died of hemorrhage through a small injury to the longitudinal sinus, we left a long bridge of bone to protect it.

Now the dura which had been left intact thus far was lightly cut and grasped with the forceps and laid back to the edge of the skull. Hereupon the dog expressed violent pain by whining and characteristic twitchings.

But later when it had been exposed to the air for a longer time, the remainder of the dura mater was rendered far more sensitive, a circumstance which, in carrying out the experiment, had to be taken carefully into consideration. However we could shock, in any degree, the pia through mechanical or any other irritation, without the animal manifesting sensation."

After giving a description of the electrical apparatus used, the authors continue: "The following are the results which we give as a summary of a very great number of experiments on the brain of the dog, which harmonize for the most part to the minutest detail, without describing all the experiments.

A part of the convexity of the cerebrum of the dog is motor, and another part is not motor. The motor part is placed, as it is generally expressed, more to the front, the non-motor lies toward the back.

Through the electric stimuli of the motor part, one obtains combined muscle contraction of the opposite half of the body."

(44)

Ferrier. Functions of the Brain. 1886, p. xxii.

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